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TITLE: Dietary Fat and Vitamin E in Prostate Cancer Risk among African Americans and Africans: A Case-Control Study

PRINCIPAL INVESTIGATOR: Flora A. M. Ukoli

CONTRACTING ORGANIZATION: Meharry Medical College
Nashville, TN 37208

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14. ABSTRACT 218(25.7%) African-Americans (A-A), 66(7.8%) African Migrants, and 564(66.5%) Nigerians were studied. Mean ages for 516 men with fatty-acid profile information were 57.1(9.7), 53.0(8.5), and 60.7(13.8) respectively, $p < 0.0001$. There were 59(11.5%) cases, 256(49.6%) controls, and 201(38.9%) with elevated PSA and/or enlarged prostate. Mean differences across ethnic groups for Omega-6 (Arachidonic, Linoleic, Adrenic, Docosapentaenoic, Dihomo-g-Linolenic), Omega-3 (Eicosapentaenoic (EPA), Docosahexaenoic (DHA), Alpha-Linolenic), Palmitic, Stearic, & Oleic acid were significant, $p < 0.011 - p < 0.0001$. A-A recorded the highest mean total Omega-6 fatty-acids [1132.80(264.7)], followed by African migrants [1077.86(233.4)], and Nigerians [694.52(209.1)], $p < 0.0001$. Mean Omega-3 index was respectively 2.34(1.2), 4.12(1.8), and 3.88(1.9), $p < 0.0001$. PCa cases had higher mean Omega-6 fatty acid, $p < 0.07$, odds ratio for PCa risk was 3.4 (95%CI 2.4 - 4.4) between the upper and lower quartile. The BMI for A-As, Migrants and Nigerians was 28.6(6.1), 28.5(4.0), and 23(4.0) respectively. Only 6.1% A-A recorded Omega-3 index $\geq 8\%$, compared to 37.9% and 36.9% for Migrants and Nigerians. Improving Omega-3 index is particular urgent for cardio-protection as well as PCa risk reduction. Dietary assessment data is yet to be analyzed.					
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INTRODUCTION:

[Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.]

A pilot study to investigate prostate cancer dietary risk factors was initiated at the Howard University Cancer Center, Washington DC, in 2000, and recruited study participants from rural Nigeria. In 2002 the scope of the study was expanded to include African-Americans and African migrants in the United States so as to investigate the role of dietary nutrients associated with increased prostate cancer risk (fatty acids) and antioxidants associated with reduced risk for prostate cancer (vitamin E), and to study how the process of migration may impact exposure to dietary risk factors for this cancer. African-Americans and African migrants study participants were recruited from the Washington D.C. metropolitan area while Nigerians were recruited from two rural and two urban communities, the health centers situated there, and one referral hospital. IRB approvals were obtained both from Howard University and the University of Benin Teaching Hospital, Nigeria.

In 2003 the PI moved to Meharry Medical College, and this grant was transferred from Howard University Cancer Center. New consent forms were developed and IRB approval were obtained from this institution. Nigerian participants continued to be recruited as in the past while African-American and African migrants were recruited from Nashville, TN. The study protocol, survey, and procedures remained the same. The main objective of the study is to locate prostate cancer cases and select community based controls who were from the same socio-economic status and age groups in both countries in a case-control design. The various demographic, medical history, dietary patterns, and nutrient levels will be compared between cases and controls to determine the fatty acid risk factors for prostate cancer among men of African ancestry in both countries. The specific nutrients of interest are fatty acids some of which have been proposed as risk factors for prostate carcinogenesis, and vitamin E, a protective antioxidant. Food items of interest include dairy products, dietary supplements, fruits, vegetables, meat and fish.

This pilot study is intended to collect and store blood and urine samples from consenting participants that will be utilized to generate pilot data to apply for funds to investigate other biomarkers and genes of interest in prostate cancer risk. The dietary style data collected in this study will also form the basis for developing a food frequency tool that will be appropriate for a comparative study across cultures with diverse eating styles.

BODY:

*[This section of the report shall describe the research accomplishments associated with each task outlined in the **approved** Statement Of Work. Data presentation shall be comprehensive in providing a complete record of the research findings for the period of the report. Appended publications and/or presentations **may** be substituted for detailed descriptions but **must** be referenced in the body of the report. If applicable, for each task outlined in the Statement of Work, reference appended publications and/or presentations for details of result findings and tables and/or figures. The report shall include negative as well as positive findings. Include problems in accomplishing any of the tasks. Statistical tests of significance shall be applied to all data whenever possible. Figures and graphs referenced in the text may be embedded in the text or appended. Figures and graphs can also be referenced in the text and appended to a publication. Recommended changes or future work to better address the research topic may also be included, although changes to the original Statement of Work **must** be approved by the Grants Officer. This approval must be obtained prior to initiating any change to the original Statement of Work.]*

Statement of Work:

Task 1 Hire research assistant. Completed.

Howard University Cancer Center.

A part-time graduate student research assistants were hired at the onset of the study.

Meharry Medical College

A full-time research assistant was hired at the onset of the study in 2003.

Task 2 Start-Up Phase and Plan Development Completed

Howard University Cancer Center:

Urologists:

We developed methods of recruiting newly diagnosed prostate cancer cases and men with elevated PSA from our prostate cancer screening program, and from the offices of Aaron Jackson, MD, C. Aghaghotu, MD, and other urologists in the community who consented to display our study flyer in their offices.

Network:

We developed and maintained strong community ties with various churches in the Washington area, including Maryland and Virginia. Our team requested invitation to give prostate cancer health talks at several churches and several community health fairs. A collaborative partnership was formed with a community based group, Assembly of Petworth, Mr. Michael Bridgewater, coordinator, who was able to link this group with the community.

The PI also patterned with the American Cancer Society (local representative Zaida Morris) to work in the community helping to educate African-American men within their 'Man-to-Man' program. A prostate cancer support group, USTOO Howard University Chapter, was also initiated to provide support and education for men who received abnormal prostate cancer screening results or who had been diagnosed with prostate cancer.

The study and the prostate cancer screening program were advertised separately on local radio channels.

IRB approval and renewal.

-Initial IRB: June 4, 2002.

-Consent form approvals:

November 6, 2002, Renewed November 6, 2003.

-IRB from University of Benin Teaching Hospital: August 1, 2002.

Meharry Medical College:

Urologists:

We continue to develop efficient methods of recruiting newly diagnosed prostate cancer cases and men with elevated PSA from urologists at Vanderbilt (Dr. Joseph Smith, and Dr. Michael Cookson), and from Urology Associates (private group) in Nashville. At the Nashville General Hospital the surgeons who consult in the surgical out-patient display the study brochure and mention the study to eligible men.

In partnership with the TN state cancer register we mailed study brochures to prostate cancer cases asking them to contact us if interested in participating in the study.

Network:

The PI initiated and maintained strong community ties with the Interdenominational Misters Forum (IMF) and local churches. Students in the Meharry MSPH program have also been engaged in outreach activity with churches as part of their practical Epidemiology experience.

The PI has registered a prostate cancer support group, USTOO Meharry, and is scheduled to meet monthly to provide information to prostate cancer cases, their families, and anyone who is interested in knowing about the disease. This group just conducted a pertaining briefing of community representatives, and has scheduled a community-based prostate cancer support group workshop for April 2007. We continue to advertise and provide free prostate cancer screening on request, at the Department of Surgery, Nashville General Hospital, and we provided screening at 5 community-based health fairs, including a 'Men's Health day at the Nashville Department of Health.

IRB approval and renewal:

-April 6, 2006: Obtained IRB renewal from Meharry IRB.

-July 31, 2006 Obtained IRB renewal from UBTH, Nigeria.

-September 20, 2006: Obtained IRB approval from the State of Tennessee Bureau of Health Services (State Cancer Registry). We mailed out over 300 study invitation letters to cases diagnosed between 2002 -2005, and we contacted about half of them whose telephone numbers were still current, and either spoke to them or left messages for them to call us.

Task 3	<u>Training Research Assistants</u>	Completed
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Howard University Cancer Center:

Graduate research assistants were trained to manage and enter data collected into the database.

Claire Tay and Rebecca Kiziri-Mayengo. 2002

Meharry Medical College:

Angelica Keng, MPH. 2003/2004

Jennifer Murphy, MSPH student. 2004/2005

Libnir Telusca, MSPH. 2006/2007

These research assistants were trained to consent and interview participants, and to manage and enter data collected. They were also trained to order supplies, arrange meetings, and assist in handling and shipping biological samples. They were trained to conduct community outreach, conduct prostate health education, recruit study participants from the church, the cancer register,

and the community at large, and to correspond with them by phone and mail. They were also responsible for mailing out prostate test results.

Research assistants were required to undergo human subject protection certification, they were trained to make professional telephone contacts to secure participants cooperation, schedule study visits, handle, label, store and ship research samples.

Task 4. Subject Recruitment:

Table i) Participant recruitment into the study by year and study site

Study Site	Existing Data	Current Report Period 2002 - 2007					2007 New Study	Total
	1999 – 2001	2002	2003	2005	2006	2007		
Rural Nigeria	111		42					153
Rural Nigeria	23							23
Urban Nigeria	91							91
Rural Nigeria (Hospital)	42		14	19				75
Rural Nigeria	16							16
Urban Nigeria Hospital	86		10	82		21	51	250
Rural Nigeria (Hospital)	8							8
Rural Nigeria	67							67
Nashville TN				83	80		30	193
Washington DC	57	55	15					127
Total	501	55	81	184	80	21	81	1003

Classification of study participants by prostate status for each study site and period:

During the proposed study period a total of 922 participants were recruited and consented. These participants have been entered into the existing database that began in 1999 from two previous pilot/feasibility studies of African-migrants in the Washington DC area, and rural Nigerians. Having been funded to conduct a pilot study to investigate the role of lycopene in prostate cancer risk, we continue to collect data shown in the table above as “2007 New Study”. Although our main focus at this time is to recruit men diagnosed with prostate cancer, we continue to recruit both cases and controls, some of the controls being potential cases given that they have elevated PSA. The next set of tables will show the number of cases, controls and potential cases for African-American men recruited from Washington DC, African-American men recruited from Nashville, African migrants recruited in Washington DC and Nashville, and Nigerians recruited

from rural and urban communities / health centers and from the general surgery and urology clinics at the University of Benin Teaching Hospital (UBTH).

Table ii) African-American study participants recruited in Washington DC metropolitan area in 2002 and 2003:

	STUDY YEAR		Total
	2002	2003	
CASES	15	5	20
CONTROLS	9	6	15
Elevated PSA	22	4	26
Total	46	15	61

Table iii) African migrant study participants recruited in Washington DC metropolitan area in 2000 and 2002

	STUDY YEAR		Total
	* 2000 Prior study	2002	
CASES	5	5	10
CONTROLS	46	1	47
Elevated PSA	5	3	8
N/A	1		1
Total	57	9	66

* Data collected within a prior pilot study that formed the basis for developing the current study.

Table iv) African-American study participants recruited in Nashville from 2004 to date.

	STUDY YEAR			Total
	2005	2006	2007	
CASES	4	14	13	31
CONTROLS	74	57	10	141
Elevated PSA	1	9	1	11
N/A		5		5
Total	79	85	24	188

Table v) African Migrant study participants recruited in Nashville from 2004 to date

	STUDY YEAR		Total
	2005	2006	
CASES	0	0	0
CONTROLS	3	1	4
N/A	1		1
Total	4	1	5

Table vi) All African Migrant study participants recruited in Washington DC and Nashville.

	STUDY YEAR				Total
	2000	2002	2005	2006	
CASES	5	5			10
CONTROLS	46	1	3	1	51
Elevated PSA	5	3			8
N/A	1		1		2
Total	57	9	4	1	71

Table vii) All Nigerian study participants recruited into the study from 2 Rural, 2 Urban, and 2 Health Centers and Hospitals in Southern Nigeria

	*Prior studies			Report Period			Total
	1999	2000	2001	2003	2005/06	2006/07	
CASES	15	32	21	13	29	35	145
CONTROLS	53	158	71	39	43	17	381
Elevated PSA	1	30	14	7	19	10	81
N/A	6	7	36	7	10		66
Total	75	227	142	66	101	62	673

* Data collected within a prior pilot study that formed the basis for developing the current study.

Task 5. Interim Data Analysis

Completed

Data Base:

The study data is stored in SPSS version 14.6, and the data has not been transferred to an updated version of the program. The various data collected to date has been entered into the data base as follows:

Survey Sections	Collected & Entered	Comments
Personal Information	982	Completed interviews were entered in the data base.
Dietary Assessment	947	
Anthropometrics	910	
Modified FFQ (SPSS database)	529	
Free Fatty Acid	575	All laboratory analysis entered in data base.
Lipid Panel	436	
Vitamin E	112	Stored sample stored for future studies.
Testosterone	131	

So far data analysis has resulted in a couple of manuscripts, various oral presentations, and poster presentations listed below in Task 6.

Specialized Data Analysis:

Ongoing

This project has accumulated data that will generate several manuscripts on an ongoing basis as materials from more advanced statistical analysis become available.

Task 6. Report Writing and Presentations (18 - 24 months)

Oral Presentations:

2007:

A prostate cancer screening program for low-income African-American men in Nashville. Ninth HBCU and HIS Health Services Research Conference. "Improving Health Outcomes and Health Disparities: Research and Intervention Perspectives. New Orleans, LA. December 6 – 7, 2007.

Dietary fatty acids and prostate cancer risk in Nigerians. A case-control study. Sixth AORTIC conference. CTI Conference Center, Cape Town, South Africa. 24-28th October 2007.

Dietary fat and prostate cancer risk among African-Americans and Africans: A case-control study. IMPaCT Meeting. Department of Defense. Atlanta GA. September 2007.

2006:

Dietary Determinants of Prostate Cancer in Black Populations. July 2006. LSU. New Orleans.

Response to Prostate Biopsy by Nigerian men: Community and Hospital Experience. July 9 -12. 2006. UICC World Cancer Congress, Washington DC.

2005:

Recruiting Minorities for Prostate Cancer Research with Respect, Beneficence and Justice. The 29th Annual Matthew Walker Surgical Symposium & The 58th Annual Hale-McMillan Heritage Lecture. 2005. Meharry Medical College, Nashville TN.

2004:

Community based prostate cancer dietary risk study: Recruiting African Americans and Africans through a screening program. Spring 2004 Seminar Series. North Carolina Central University, Durham.

2003:

Screening for prostate cancer: Positive attitude and response by African American men. Presented at the 18th Annual Howard University College of Medicine Resident/Faculty Scientific Research Forum. 2003.

Abstracts and Posters:

2002:

Flora A. M. Ukoli, Folasade Akereyeni, Efosa Iyamu, Peter Oside, Eruke Egbagbe, Dale Young, Rick Kittles, Usifo Osime, Lucile L. Adams-Campbell. Undiagnosed prostate cancer in southern Nigeria: prevalence of disease risk. 2002. American College of Epidemiology. Annual Scientific Conference. Albuquerque, New Mexico. (Abstract)

2006:

UICC (International Union Against Cancer) World Cancer Congress. Washington DC.

1. Akumabor P.N, Aligbe J.U, Ukoli F.A. Management of Prostate Cancer Among Patients Presenting with Prostatic Disease in a Single Urology Practice in Southern Nigeria. (Abstract accepted)
2. Adekanyan A, Onawola K, Obarisiagbon E, Oguike T, Akumabor P, Ukoli F. Onuora V. Digitally Guided Transrectal Biopsy Of The Prostate (Abstract accepted)

2007:

Khandaker A. Taher, Rodney Davis, Carlton Z. Aams, Philip Akumabor, Usifo Osime, Flora A. M. Ukoli. A comparative study of serum linoleic acid in prostate cancer risk between African Americans and Africans. American Association for Cancer Research. First AACR Conference: The Science of Cancer Health Disparities. November 2007. Atlanta GA. **Recipient of AACR-Astra Zeneca Scholar-in-Training Award.**

Khandaker A. Taher, Temple Oguike, Usifo Osime, Derrick Beech, Michael S. Cookson, Flora A.M. Ukoli. A comparative evaluation of the fatty acid profiles of African-Americans and

Africans: Implication for prostate cancer risk. African Organization for Research and Training in Cancer (AORTIC) 2007. October 2007. Capetown, South Africa.

Publications:

Publications from this study:

1. Flora A. Ukoli, Eruke Egbagbe, Barbara B. Zhao, Efosa Iyamu, Dale Young, Philip Osime, Usifo Osime, Lucile L. Adams-Campbell. Anthropometric Body Fat Predictors of Elevated Prostate Specific Antigen among Rural and Urban Nigerians: A Population-Based Study. *WJOM*. 2007; 26(1):7-13.
2. F.A. Ukoli, E Egbagbe, F. Akereyeni, E. Iyamu, T. Oguike, P. Akumabor, and U. Osime. Response to Prostate Biopsy by Nigerian men: Community and Hospital Experience. Proceedings of the UICC World Cancer Congress, Washington D.C.(USA), July 8-12. 2006. Pgs 341- 347. Medimond. International Proceedings.
3. F. Ukoli, U. Osime, F. Akereyeni, O. Okunzuwa, R. Kittles, L. Adams-Campbell. Prevalence of Elevated Serum Prostate Specific Antigen in Rural Nigeria. *International Journal of Urology*. 2003; 10:315-322.

Prostate cancer publications in collaboration with other researchers.

4. Fowke JH, Signorello LB, Underwood W 3rd, Ukoli FA, Blot WJ. Obesity and prostate cancer screening among African-American and Caucasian men. *Prostate*. 2006.
5. Fowke, J.H., Signorello, L, Chang, S, Matthews, C.E, Buchowski, M., Cookson, M. Ukoli, F., Blot, W. Effects of Obesity and Height on PSA and Percent Free PSA Levels Among African-American and Caucasian Men. *Cancer*. (2006, in press.)
6. Flora Ukoli, Barlow Lynch, Lucile Adams-Campbell. The effect of radical prostatectomy on patient quality of life in African Americans. *Ethn Dis*. 2006;16:988-993.
7. Odedina FT, Ogunbiyi JO, Ukoli FA. Roots of prostate cancer in African-American men. *J Natl Med Assoc*. 2006 Apr;98(4):539-43.
8. Fowke, J.H., Schlundt, D., Signorello, L.B., Ukoli, F.A.M., Blot, W.J. Prostate cancer screening among low-income African-American and Caucasian men. *Urologic Oncology: Seminars and Original Investigation*. 2005;23:333-340.
9. Panguluri RC, Long LO, Chen W, Wang S, Coulibaly A, Ukoli F, Jackson A, Weinrich S, Ahaghotu C, Isaacs W, Kittles RA. COX-2 gene promoter haplotypes and prostate cancer risk. *Carcinogenesis*. 2004 Jan 30.
10. Kittles RA, Chen W, Panguluri RK, Ahaghotu C, Jackson A, Adebamowo CA, Griffin R, Williams T, Ukoli F, Adams-Campbell L, Kwagyan J, Isaacs W, Freeman V and Dunston GM. CYP3A4-V and prostate cancer in African Americans: causal or confounding association because of population stratification. *Hum Genet*. 2002, 110:553-560.

KEY RESEARCH ACCOMPLISHMENTS:

[Bulleted list of key research accomplishments emanating from this research.]

Nigerian Site:

1. More men with abnormal prostate cancer screening, and very high PSA levels, several above 100ng/ml, and a few above the 1,000ng/ml mark, one participant recording a PSA of 14,000ng/ml. continue to be identified. We are looking very seriously at this situation, trying to work with our partners there to begin community-based prostate cancer awareness.
2. Men diagnosed with prostate cancer are receiving usual medical treatment. Almost all of them are diagnosed with disease that is not local.
3. Men are receiving information about prostate cancer, the meaning of the PSA test, and the available of treatment options for organ confined prostate cancer detected early.
4. Laboratory analysis budgeted for this study has been completed.

Nashville Site:

1. The very active community outreach and presence that has been achieved needs to be maintained so as not to loose momentum.
2. Recruitment emphasis has changed to cases both from the cancer registry and from urology offices. Future studies will have to develop methods for recruiting men at diagnosis.
3. This study has provided prostate cancer screening for men in the community, some of whom did not want to participate in the study.
4. Data entry is completed for personal information and diet assessment. Data for the food frequency questionnaire is still ongoing.
5. Laboratory analysis budgeted for this study has been completed.

Washington DC Site:

1. A very active community outreach presence was established and maintained through the activities of this study. This has now grown and developed into a very impressive and successful prostate cancer program.
2. Although the PI moved from the HUCC to Meharry African-American and African migrant men in that community have come to understand the need, importance, and safety for them to participate in epidemiological studies such as this. Recruitment into other studies will therefore be a lot easier than in the past.
3. This study has provided prostate cancer screening for over 3,000 men from the community, some of whom did not want to participate in the study. Participating in the study was not a prerequisite for getting a free prostate cancer screening.
4. Data entry is completed for personal information, diet assessment, and up to 80% of the “modified BLOCK” food frequency questionnaire.
5. Laboratory analysis budgeted for this study has been completed.

REPORTABLE OUTCOMES:

[Provide a list of reportable outcomes that have resulted from this research to include:]

1. Abstracts: 3
2. Posters: 3
3. Publications: 3
4. Community Network established in Washington DC, Nashville, and Nigeria.
5. Community partnership maintained with over 20 church communities, local associations, and health centers in Nashville.
6. Partnership with other centers, such as the clinical research center (CRC) at Meharry continues to be active.
7. Community network continues to be maintained in Nigeria. The program director (Usifo Osime) and the two study urologists continue to provide their support for the study.
8. Collected demographic and dietary assessment information for over 900 participants.
9. Collected and stored plasma, serum, cell, clot and urine samples for over 800 men.
10. Created a database of almost 1,000 and over 800 primary variables and an additional 50 computed variables.

CHALLENGES:

Nigerian Site:

- 1 Prostate biopsy in Nigeria:
 - a. Men with or without symptoms, who have elevated PSA, are still uncomfortable and not accepting to undergo prostate biopsy. The urologists do counsel them and leave them to make up their mind if they will undergo the procedure.
 - b. Urologists will need an ultrasound equipment to collect better biopsy samples.
- 2 Biopsy samples were obtained from some prostate cancer cases who promised to return to complete the study survey after 3 months. Efforts to reach these men have not been successful. At least 6 of these men were traced to their homes, and are said to be diseased.
- 3 The study did not budget adequately for the urologists. There is need to include junior investigators in the study and to provide budgetary compensations for them as they are a very necessary part of the research team.

Nashville Site:

- 1 Cases: Although the study secured the support of private urologists in the community, and urologists at the Vanderbilt University Medical Center, recruiting from these offices have been very complex. It may be necessary to budget for part-time research nurse coordinator at sites where the study expects to recruit cases. That individual will then be responsible to recruit study participants. Recruiting recently diagnosed prostate cancer cases will depend on the support of the urologists and their office staff.

- 2 Controls: The need to reach participants with their results means that the study may have to recruit only men with an address. The 'Homeless' is very difficult to follow-up, and prostate cancer may be the least of their immediate problems. Several of the results returned in the mail are for such men.
- 3 Cash Incentive: It appears as if the importance of research such as this is not understood by many, such that they are not willing to make any sacrifice to participate. \$30.00 incentive appears to attract only the unemployed, and those who are on wages cannot miss a day's work for \$30.00. Only the very enthusiastic full-time employed men, who have full health insurance coverage are willing to make such a sacrifice. A minimum of \$80 (approximately \$10/hour for one day missed earning) will be proposed in future studies.
- 4 Research staff: A study such as this should budget for a full-time study nurse coordinator, a full-time research assistant, and a full-time laboratory assistant, otherwise the PI is over stretched taking up some of the responsibilities.
- 5 Research Laboratory: It is important for this study to develop a research laboratory that will be able to assay nutrients of interests such as fatty-acids, vitamin E, and other antioxidants relevant to prostate cancer risk. The service cost for these assays are very high. Support of existing core laboratories, willing and able to assay these specific nutrients, must be secured. The study budget must therefore include a full-time laboratory technician for this purpose.
- 6 Data analysis is particularly difficult when the statistician has to deal with PI designed survey tools particularly when the statistician was not involved in the development of the said survey. This is especially troublesome in this study that is utilizing an unfamiliar survey tool, the 'modified BLOCK' food frequency questionnaire developed to capture this cross-cultural eating pattern. The new statistician at Meharry is willing to collaborate with the PI to work on this. It should be noted that analysis of this section of the project was not included in the study task.

CONCLUSIONS:

[Summarize the results to include the Importance and/or implications of the completed research and when necessary, recommend changes on future work to better address the problem. A "so what section" which evaluates the knowledge as a scientific or medical product shall also be included in the conclusion of the report.]

The study has met its recruitment goals in Nigeria but not in the United States. The study was able to meet its recruitment goal for African-American controls both in Washington DC and in Nashville, however recruitment goal for cases was not met in either site. Recruiting African migrants was particularly challenging most especially in Nashville. The study did not meet the recruitment goal for this group at all.

The study did not meet its accrual target because active accrual of cases started very late into the study, and prostate cancer cases are not particularly easy to recruit into studies. There is also a need to develop a better method of securing the support of physicians and urologists who occupy a very important position of bringing the study to the notice of their patients. Media exposure in local newspapers, newsletters, radio and television, must continue throughout the study period, and there is need to adequately budget for that. The cash incentive for study participants should be increased to about \$80 to cover the lost of 'lost-wages' due to skipping work to participate in the study.

In Nigeria, public knowledge about cancer in general, and prostate cancer in particular, is low. Although many people accepted to participate in research, the fear of the unfamiliar prostate biopsy procedure was overwhelming. The fear of a positive cancer diagnosis is also a deterrent. There is urgent need for public campaign about cancer / prostate cancer. Exceeding our recruitment goal for controls was a very efficient opportunity for prostate cancer case finding, who can then be encouraged to complete the process of diagnosis.

This study confirms the feasibility of a case-control study to compare prostate cancer nutrition epidemiology among men of African ancestry across two continents, providing ample pilot data. Small grants can be secured to analyze stored biological samples and the data collected so as to generate pilot data to source for more substantial external funding to increase the sample size and statistical power. Such grants must take into cognizance the need for a multidisciplinary team of basic scientists, clinicians, epidemiologists, and other community-based researchers. Adequate budgetary allocation should always be included in studies such as this to meet the cost of a well equipped and staffed research laboratory to allow for in-house sample analysis.

Data Analysis Summary:

Response among prostate cancer cases was much better among Nigerians compared to the African-Americans, while response by controls was very good in both sites. The Nigerian prostate cancer cases were diagnosed in the late stages with numerous symptoms, because they presented late while the US cases were detected mainly by PSA screening in the early stage. Nigerians who had elevated PSA avoided prostate biopsy out of fear. Dietary pattern between both populations was different particularly regarding serving portions. Nigerians ate larger portions of carbohydrates such as rice, corn and cassava, while bread was commonly reported in the African-American diet, but not the Nigerian one. Fish was the most popular choice of Nigerians, followed by beef, while Chicken and beef was more popular among African-Americans. African-Americans ate butter and margarine while the source of fat in the Nigerians diet was mainly vegetable oil, particular palm oil. In general African-Americans ate larger portions of meat and fish compared to Nigerians. These dietary patterns were reflected in their fatty acid profiles, African-Americans recording higher levels of total and omega-6 fatty acids while Nigerians recorded higher saturated and omega-3 fatty acids. Preliminary results indicate that red meat and Omega-6 fatty acid are both associated modestly with increased prostate cancer risk among the Nigerians only. Fish and Omega-3 was not associated with prostate cancer risk in either population. These preliminary results will be confirmed in a larger sample size once the food frequency data is completed entered into the data base, and when additional fund is secured to complete fatty acid assay of stored samples of cases and controls from both study sites. Grant proposals for future research will be developed to assay other nutrients in the stored samples such that interactions between fatty acids and protective nutrients (antioxidants) can be studied.

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APPENDIX A:

Data Analysis: (This section is limited to 848 participants who provided a blood sample)

Site

Recruitment Site	Ethno-Cultural Group			Total	
	African-American	African-Migrants	African (Nigeria)	N	%
House-To-House			305 (54.1)	341	36.0
Church	16 (7.3)			16	1.9
Urologist Office			232 (41.1)	232	27.4
Recreation Club			27 (4.8)	27	3.2
Screening Program	190 (87.2)	64 (97.0)	21 (3.3)	254	30.0
Cancer Register	12 (5.5)	2 (3.0)		14	1.7
TOTAL	218	66	564	848	

Table 1:
Study
Participants
Recruitment
by Ethno-
Cultural Group

Table 2(a) Birth Place of 218 African-American Study Participants:
(Washington DC & Nashville)

TN 122
DC 22
VA 11
AL 7
NC 7
SC 6
MI 5
NY 5
GA 4
MS 4
KY 3
IL 3
PA 3
KS 2
FL 2
AK 1
A 1

Southern region of the United States includes 16 states

- The South Atlantic States: Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia and West Virginia (plus the District of Columbia)
- The East South Central States: Alabama, Kentucky, Mississippi and Tennessee
- The West South Central States: Arkansas, Louisiana, Oklahoma and Texas.

East South Central States	136
South Atlantic States	53
West South Central States	3
Others	24
Undisclosed	2
Total	218

IA	1
LA	1
LO	1
MD	1
MO	1
MT	1
OH	1
TX	1
USA	2

Table 2(b) Birth Place of 66 African Migrant Study Participants: (Washington DC & Nashville)

Nigeria	35	(16 Yoruba states, 12 undeclared, 7 southern)
Ghana	13	
Cameroon	5	
Ethiopia	3	
Liberia	2	
Sierra-Leone	2	
Kenya	2	
Benin Republic	1	
Others	3	

Table 2(c) Birth Place of 564 Nigerian Study Participants: (Nigeria.)

Edo State	275(48.8)	
Delta State	172(30.5)	
Adjacent States	41	Adjacent to Edo & Delta
Bauchi	36	
Plateau	11	
Other Southern	11	(East=9, West=5)
Northern States	8	
Undeclared	5	
Other Countries	2	
Total	564	

Edo State	275
Delta State	172
Other Southern States	55
Bauchi- Plateau States	47
Northern States	8
Undeclared	5
Other Countries	2
Total	564

Table 3: Classification of Study Participants by Status of Prostate Health by Ethno-Cultural Group

	Ethno-Cultural Group			Total	
	African-American	African Migrant	African (Nigeria)		
CASES	38(17.4)	10(15.2)	66(11.7)	114	13.4
CONTROLS	127(58.3)	40(60.6)	241(42.7)	408	48.1
Elevated PSA (Normal DRE)	16(7.4)	5(7.6)	43(7.6)	64	7.6
Biopsy negative	5(2.3)			5	0.6
Elevated PSA + BPH	14(6.4)	3(4.5)	58(10.3)	75	8.8
BPH only	17(7.8)	8(12.1)	132(23.4)	157	18.5
PIN, Basal Cell proliferation etc.			6(1.1)	6	0.7
Prostatitis (Chronic & Acute)	1(0.5)		6(1.1)	7	0.8
Highly suspicious of Prostate Cancer			11(2.0)	11	1.3
Others			1(0.2)	1	0.1
	218	66	564	848	

Table 4: Age Distribution of Study Participants by Ethno-Cultural Group

Age Group	Ethno-Cultural Group			Total	
	African-American	African Migrant	African (Nigeria)		
< 55	107(49.1)	39(59.1)	187(33.2)	333	39.3
55 - 64	68(31.2)	21(31.8)	151(26.8)	240	28.3
65 - 74	30(13.8)	6(9.1)	139(24.6)	175	20.6
75 - 84	13(6.0)		66(11.7)	79	9.3
>= 85			21(3.7)	21	2.5
	218	66	564	848	

P<0.000

Table 5: Education Status of Participants By Ethno-Cultural Group

Education	American, Migrant, African			Total N %	
	African-American	Migrant African	African (Nigeria)		
< 6 th Grade (Primary)		1(1.6)	155(28.3)	156	18.9
6 – 9 th Grade (Jnr. Secondary)	28(13.1)	3(4.9)	209(38.1)	240	29.2
12 th Grade (Secondary)	94(43.9)	4(6.6)	69(12.6)	167	20.3
Post Secondary Training	23(10.7)	1(1.6)	52(9.5)	76	9.2
College Degree	44(20.6)	21(34.4)	52(9.5)	117	14.2
Postgraduate	25(11.7)	31(50.8)	11(2.0)	67	8.1
Total	214	61	548	823	
Not Recorded	4	5	16	25	

Table 6: Marital Status by Ethno-Cultural Group

Marital Status	American, Migrant, African			Total N %	
	African-American	African Migrant	African (Nigeria)		
Single	70(32.3)	4(6.5)	8(1.4)	83	9.5
Married	62(28.5)	43(70.5)	373(66.4)	510	58.2
Divorced or Separated	57(26.3)	9(14.8)	27(4.8)	94	10.7
Widowed	15(6.9)		12(2.1)	28	3.2
Remarried	13(6.0)	5(8.2)	141(25.1)*	162	18.4
Total	217	61	562	840	
Not Recorded	1	5	2	8	

*Remarried (Nigeria): Married ≥ 2 times as a result of polygamy, widowhood, or divorce.

Table 7: Number of Children by Ethno-Cultural Group

Number of Children	American, Migrant, African			Total N %	
	African-American	African Migrant	African (Nigeria)		
None	43(19.7)	2(3.0)	12(2.1)	57	6.7
1 or 2	79(36.2)	12(18.2)	54(9.6)	145	17.1
3 or 4	61(28.0)	21(31.8)	80(14.2)	162	19.1
5 – 9	28(12.8)	23(34.8)	248(44.0)	299	35.3
10 – 19	2(0.9)	1(1.5)	142(25.2)	145	17.1
>= 20			21(3.7)	21	2.5
Not Recorded	5(2.3)	7(10.6)	7(1.2)	19	2.2
	218	66	564	848	

Table 8: Current Job Status by Ethno-Cultural Group

Job Status	American, Migrant, African			Total N %	
	African-American	African Migrant	African (Nigeria)		
Not Working	36(16.7)	5(8.2)	48(8.5)	89	10.7
Retired	57(26.5)	5(8.2)	165(29.3)	227	27.1
Employed (Part-Time)	35(16.3)	9(14.8)	34(6.1)	78	9.5
Employed (Full-Time)	60(27.9)	41(67.2)	276(49.0)	377	44.9
Disabled Unable To Work	24(11.2)	1(1.6)	2(0.4)	27	3.2
Self Employed	3(1.4)		38(6.7)	41	4.9
	215	61	563	839	
Not Recorded	3	5	1	9	

Table 9: Type of Occupation by Ethno-Cultural group

Job Description	American, Migrant, African			Total N %	
	African-American	African Migrant	African (Nigeria)		
Managerial & Professional	51(26.8)	37(61.7)	101(19.5)	189	24.6
Technical, Sales, Admin. Support	34(17.9)	10(16.7)	75(14.5)	119	15.5
Service	40(21.1)	10(16.7)	87(16.8)	137	15.9
Operators, Farmers/Laborers	65(34.2)	3(5.0)	254(49.1)	322	42.0
	190	60	517	767	
Not Stated	28(12.8)	6(9.1)	47(8.3)	81	(9.6)
Total	218	66	564	848	

Table 10: Distribution of Participants by Income Group for Each Ethno-Cultural Group

Income Group (Dollar/Naira)	American, Migrant, African			Total N %	
	African-American	African Migrant	African (Nigeria)		
<\$10,000	81(38.6)	6(11.5)	291(58.9)	378	50.0
\$10,000-\$24,999	39(18.6)	9(17.3)	75(15.2)	123	16.3
\$25,000-\$34,999	18(8.6)	8(15.4)	42(8.5)	68	9.0
\$35,000-\$49,999	25(11.9)	4(7.7)	26(5.3)	55	7.3
\$50,000-\$74,999	22(10.5)	12(23.1)	7(1.4)	41	5.4
\$75,000-\$99,999	17(8.1)	6(11.5)	13(2.6)	36	4.8
>= \$100,000	8(3.8)	7(13.5)	40(8.1)	55	7.3
Total	210	52	494	756	
Not Recorded	8	14	70	92	

Table 11:

Quartile Distribution of Computed SES Stratification Across America & Nigeria Using Education and Income Levels.

Socio-Economic Ranking	American, Migrant, African			Total N %	
	African-American	African Migrant	African (Nigeria)		
Lowest Quartile			213(43.4)	213	28.4
2 nd Quartile	26(12.5)	3(5.8)	109(22.2)	138	18.4
3 rd Quartile	110(52.9)	5(9.6)	96(19.6)	211	28.1
Highest Quartile	72(34.6)	44(84.6)	73(14.9)	189	25.2
	208	52	491	751	
Not recorded	10	14	73	97	

Table 12: Age at Puberty by Ethno-Cultural Group

Age at Puberty	American, Migrant, African			Total N %	
	African-American	African Migrant	African (Nigeria)		
=< 11	12(5.5)			12	1.4
12 – 16	154(70.6)	8(12.1)	67(11.9)	229	27.0
17 – 21	22(10.1)	4(6.1)	63(11.2)	89	10.5
>= 22	2(0.9)		23(4.1)	25	2.9
Not Collected	28(12.8)	54(81.8)	411(72.9)	493	58.1
Total	218	66	564	848	

Table 13: Health Insurance Status by Ethno-Cultural Group

Health Insurance	Ethno-Cultural Group			Total	
	African-American	African Migrant	African (Nigeria)		
Private	67(30.9)	26(51.0)		93	11.2
Medicare/Medicaid	61(28.1)			61	7.4
Veteran	22(10.1)			22	2.7
Employer reimburse	6(2.8)	1(2.0)	37(6.6)	44	5.3
No Hlth Insurance Out-of-Pocket	61(28.1)	24(47.1)	524(93.4)	609	73.5
Total	217	51	561	829	
N/R	1	15	3	19	

Table 14: Duration in Years Since Last Doctor's Visit

Years since last Doctor Visit	American, Migrant, African			Total	
	African-American	African Migrant	African (Nigeria)		
=<1	137(62.8)	24(36.4)	238(42.2)	399	47.1
2 – 4	2(0.9)	1(1.5)	46(8.2)	49	5.8
5 – 9	1(0.5)		9(1.6)	10	1.2
>= 10	78 (35.8)	41(61.2)	271(46.1)	390	46.0
Total	218	66	564	848	

Table 15: Primary Care Provider of American, Migrant & African Participants

	Ethno-Cultural Group			Total	
	African-American	African Migrant	African (Nigeria)		
None	95(43.6)	35(53.0)	223(39.5)	353	41.6
Chemist/ Traditional			8(1.4)	8	0.9

Health Center	84(38.5)	2(3.0)	193(34.2)	279	32.9
Hospital/Dr's office	39(17.9)	29(43.9)	140(24.8)	208	24.5
	218	66	564	848	

Table 16: Life-time number of PSA testing among study participants

Number PSA TEST	Ethno-Cultural Group			Total	
	African-American	African Migrant	African (Nigeria)		
NEVER	57(31.1)	30(50.0)	491(89.6)	578	73.7
ONCE	36(19.7)	13(21.7)	46(8.4)	95	11.5
2 - 4	36(19.7)	16(26.7)	10(1.8)	62	7.6
5 TO 10	17(9.3)			17	2.0
>= 11	31(16.9)	1(1.7)	1(0.2)	33	4.0
Don't Know	41(3.3)	6	16(0.7)	63	1.2
Total	218	66	564	848	

Table 17: History of Previous DRE among Study Participants

Previous DRE	Ethno-Cultural Group			Total	
	African-American	African Migrant	African (Nigeria)		
NO	65(29.8)	34(51.5)	420(74.5)	519	61.2
YES	153(70.2)	32(48.5)	144(25.5)	329	38.8
Total	218	66	564	848	

Table 18: Previous DRE Finding among Study Participants by Ethno-Cultural Group

DRE Result	Ethno-Cultural Group			Total	
	African-American	African Migrant	African (Nigeria)		
Normal	93(60.8)	18(56.3)	10(6.9)	121	36.8
Enlarged	26(17.0)	3(9.4)	42(29.2)	71	21.6
Cancer Suspected	8(5.2)	1(3.1)	17(11.8)	26	7.9
Prostatitis	2(1.3)	4(12.5)	1(0.2)	7	2.1
Don't Know	24(15.7)	6(18.8)	74(51.4)	104	31.6

Total	153	32	144	329

Table 19(a): Prostate Status on Current DRE of Study Participants by Ethno-Cultural Group

DRE Result (Current)	Ethno-Cultural Group			Total	
	African-American	African Migrant	African (Nigeria)		
Normal	88(40.4)	20(30.3)	248(44.0)	356	42.0
BPH No Symptom	15(6.9)	3(4.5)	103(18.3)	121	14.3
BPH Symptoms	8(3.7)	8(12.1)	104(18.4)	120	14.2
Abnormal (Cancer Suspected)	3(1.4)	1(1.5)	48(8.5)	52	6.1
Not Done/ Don't Know	104(47.7)	34(51.5)	61(10.8)	199	23.5
Total	218	66	564	848	

Table 19(b) Prostate Status on Current DRE for Nigerian Participants by Recruitment Site

DRE Result	RECRUITMENT			Total	
	HOUSE-TO-HOUSE	UROLOGY CLINIC	RECREATION CLUB		
Normal	179(58.7)	54(23.3)	15(55.6)	248	44.0
BPH No Symptom	87(28.5)	13(5.6)	3(11.1)	103	18.3
BPH With Symptom	23(7.5)	81(34.9)		104	18.4
Abnormal Cancer Suspected	6(2.0)	42(18.1)		48	8.5
Not Done/ Don't Know	10(3.3)	42(18.1)	9(33.3)	61	10.8
Total	328	232	27	564	

Table 19(c) Prostate Status on DRE for African-American Participants by Recruitment Site

DRE Result	RECRUITMENT			Total	
	Pl's Office*	Church	Cancer Register		
Normal	74(38.9)	4(25.0)	10(83.3)	88	40.4
BPH No Symptom	15(7.9)			15	6.9
BPH With Symptom	8(4.2)			8	3.7

Abnormal Cancer Suspected	2(1.1)		1(8.3)	3	1.4
Not Done/ Don't Know	91(47.9)	12(75.0)	1(8.3)	104	47.7
Total	190	16	12	218	

* Response to flyers and advertisement on radio, television, and newspaper

Table 19(d) Prostate Status on DRE for African Migrants by Recruitment Site

DRE Result	RECRUITMENT		Total	
	PI's Office	Cancer Register		
Normal	20(31.3)		20	30.3
BPH No Symptom	3(4.7)		3	4.5
BPH With Symptom	8(12.5)		8	12.1
Abnormal Cancer Suspected	1(1.6)		1	1.5
Not Done/ Don't Know	32(50.0)	2(100.0)	34	51.5
Total	64	2	66	

Table 20: History of Urinary Symptoms among Study Participants

Urinary Symptoms	Ethno-Cultural Group			Total	
	African-American	African Migrant	African (Nigeria)		
NO	165(75.7)	54(81.8)	317(56.2)	536	63.2
YES	53(24.3)	12(18.2)	247(43.8)	312	36.8
	218	66	564	848	

Table 21: Prevalence of Urinary Symptoms among Study Participants

Urinary Symptoms	Ethno-Cultural Group			Total	
	African-American	African Migrant	African (Nigeria)		
Frequency 0.094	19.3	7.4	15.6	113	16.1
Retention* 0.005	8.3	3.7	15.3	86	12.3
Weak Stream	13.3	13.0	11.4	85	12.1

Pain*	0.000	3.2	3.7	14.2	70	10.0
Hesitancy		9.2	3.7	11.2	70	10.0
Dribbling		9.2	3.7	10.9	69	9.8
Urgency		8.7	1.9	9.8	62	8.8
Nocturia		17.4	5.6	4.9	62	8.8
Ed*		11.0	1.9	6.5	53	7.5
Straining		7.3	3.7	7.9	52	7.4
Incontinence		3.2	0	3.5	22	3.1
Haematuria		1.8	0	4.0	21	3.0
Blood in the semen		0.9	0	0.7	5	0.7
Known BPH		26.3	16.7	10.9	128	15.3
Known PCa		14.3	11.3	3.2	56	6.7
Total BPH		28.1	23.3	38.9	293	34.6
Total PCa		17.1	16.1	13.6	123	14.5

Table 22: Fatty-Acid Profile for Study Participants by Ethno-Cultural Group

Mean Total	Fatty Acids	Mean (SD)			P-val
		African-Americans	African Migrants	African (Nigerians)	
625(211)	Linoleic (LA)	793 (187)	774 (166)	517 (151)	0.000
596(196)	Palmitic	550 (175)	518 (147)	632 (205)	0.000
583(256)	Oleic	527 (227)	442 (156)	636 (269)	0.000
195(58)	Stearic	207 (64)	193 (46)	190 (56)	0.011
172(88)	Arachidonic	252 (73)	239 (69)	122 (56)	0.000
64(38)	Docosahexaenoic (DHA)	49 (24)	76 (29)	70 (43)	0.000
60(42)	Palmitoleic	47 (30)	35 (22)	70 (46)	0.000
44(27)	Vaccenic	45 (19)	38 (11)	45 (31)	0.177 ns
34(16)	Dihomo-g-LNA	43 (17)	36 (13)	30 (13)	0.000
30(10)	Nervonic	26 (6)	29 (9)	32 (10)	0.000
26(24)	Ecosapentaenoic (EPA)	16 (14)	30 (24)	31 (26)	0.000
26(21)	Myristic	20 (14)	16 (10)	31 (23)	0.000
11(11)	Alpha-Linolenic (LNA)	14 (7)	12 (5)	8 (5)	0.000
10(6)	Gamma-Linolenic (GLA)	12 (5)	12 (5)	8 (4)	0.000

Table 23: Total / Sub-Group Fatty Acid Profile for Study Participants by Ethno-Cultural Group

Mean Total	Fatty Acids	Mean (SD)			P-val
		African-Americans	African Migrants	African (Nigerians)	

2639(774)	Total Fatty Acid	2810 (800)	2607 (609)	2565 (779)	0.006
596(196)	Total Saturated	835 (241)	773 (246)	922 (294)	0.000
862(309)	Total Omega-6	1133 (265)	1078 (233)	695 (209)	0.000
640(268)	Total Omega-9	578 (241)	497 (168)	695 (280)	0.000
115(66)	Total Omega-3	96 (43)	138 (56)	120 (75)	0.000
112(61)	Total W-7&W-5	111 (55)	84 (32)	118 (66)	0.001
37(45)	Total Trans-Fat	83 (63)	46 (16)	18 (8)	0.000

Table 24 Omega3:Omega6 Ratios for Study Participants by Ethno-Cultural Group

Mean Total	Fatty Acid Ratios	Mean (SD)			P-val
		African-Americans	African Migrants	African (Nigerians)	
0.1439(.083)	Omega3:Omega-6	0.0842(.032)	0.1306(.055)	0.1746(.088)	0.000
0.1985(.201)	EPA : AA	0.0655(.070)	0.1335(.113)	0.2738(.218)	0.000
33.38(13.5)	Omega-3: -6 (HUFA)	19.88(6.72)	29.52(8.85)	40.50(11.28)	0.000
3.471(1.88)	Omega-3 Index	2.345(1.22)	4.117(1.83)	3.884(1.92)	0.000
4.366(2.03)	Omega-3: TFFA	3.415(1.32)	5.327(1.94)	4.637(2.15)	0.000
66.44(4.75)	UnSaturated Index	70.23(2.50)	70.34(5.57)	63.92(3.56)	0.000

Table 25: Fatty Acid Profile of Prostate Cancer Cases and Controls

Fatty Acids	Mean (SD)		P-val
	Cases N = 59	Controls N = 256	
Linoleic (LA)	686.15(207.1)	632.94(216.1)	0.087
Palmitic	604.29(209.2)	584.88(190.5)	
Oleic	582.99(239.4)	571.46(252.0)	
Stearic	205.93(51.6)	193.13(60.9)	0.039
Arachidonic	200.39(93.3)	173.74(88.2)	
Docosahexaenoic (DHA)	67.51(59.3)	59.34(32.5)	
Palmitoleic	51.42(30.1)	58.57(37.4)	0.077
Vaccenic	44.99(16.2)	42.22(18.6)	
Dihomo-g-LNA	34.72(12.7)	35.25(16.8)	
Nervonic	32.73(9.8)	27.12(7.7)	0.000
Ecosapentaenoic (EPA)	23.25(19.0)	25.21(22.4)	
Myristic	24.03(23.1)	25.30(16.4)	
Alpha-Linolenic (LNA)	11.71(7.8)	11.42(12.6)	
Gamma-Linolenic (GLA)	10.07(5.4)	10.91(6.6)	

Table 26: Total and Sub-Group Fatty Acid Profile for Prostate Cancer Cases and Controls

Fatty Acid Ratios	Mean (SD)		P-val
	Cases	Controls	
Omega-3 : Omega-6	0.1273(.053)	0.1379(.085)	0.035
EPA : AA	0.1664(.135)	0.1923(.199)	
Omega-3: -6 (HUFA)	31.18(10.71)	32.03(14.09)	
Omega-3 Index	3.380(1.51)	3.325(1.93)	
Omega-3: TFFA	4.294(1.72)	4.237(2.06)	
Unsaturated Index	66.98(4.30)	66.80(4.45)	

Fatty Acids	Mean (SD)		P-val
	Cases	Controls	
Total Fatty Acid	2447.39(733.3)	2617.03(792.5)	0.081
Total Saturated	909.76(290.2)	861.58(262.7)	
Total Omega-6	953.95(300.8)	874.14(319.4)	
Total Omega-9	640.26(252.8)	624.81(263.6)	
Total Omega-3	115.77(50.5)	109.58(58.5)	
Total W-7&W-5	107.67(42.3)	111.02(57.2)	
Total Trans-Fat	36.59(26.7)	44.68(53.9)	

Table 27: Omega-3: Omega-6 Fatty-Acid Ratio for Prostate Cancer Cases and Controls

APPENDIX B: Comparison of Dietary Lifestyle three months prior to data collection among African-Americans, African migrants and Nigerians.

(This section is limited to 947 participants who completed the diet assessment questionnaire: 248 African-Americans, 58 African migrants and 641 Nigerians.)

Table 1: Age distribution of study participants by ethnic subgroup.

Age (Years)	Ethnic Subgroup			Total
	African- American	African Migrant	African Nigerian	
< 54	117 (47.2)	36 (62.1)	223 (34.8)	376 (39.7)
55 - 64	78 (31.5)	19 (32.8)	170 (26.5)	267 (28.2)
65 - 74	38 (15.3)	3 (5.1)	153 (23.9)	194 (20.5)
>= 75	15 (6.0)	0	95 (14.8)	110 (11.6)
	248	58	641	947

Table 2: Pattern of consumption of meat and fish in the past three months by ethnic subgroup.

Meat & Fish:	African-American	African Migrant	African Nigerian	Total	p-value
Chicken & Turkey	240 (96.3)	54 (93.1)	494(77.1)	788 (83.2)	<0.001
Chicken Part Light meat only	62 (25.6)	10 (20.0)	48 (11.4)	120 (16.8)	< 0.001
Beef	219 (88.3)	47 (81.0)	586 (91.4)	852 (90.0)	<0.05
Hamburger	219 (88.3)	38 (65.5)	76 (11.9)	333 (35.2)	<0.001
Regular	124 (56.6)	23 (60.5)	73 (96.1)	220 (66.1)	
Lean	95 (43.4)	15 (39.5)	3 (3.9)	113 (33.9)	
Tuna & Sardines	194 (78.2)	36 (62.1)	444 (69.3)	520 (54.9)	<0.001
Water packed	122 (62.9)	16 (44.4)	9 (2.0)	147 (28.3)	
With Mayonnaise	136 (70.1)	14 (38.9)	1 (.002)	151 (29.0)	

Table 3: Pattern of milk and cereal consumption in the last three months by ethnic subgroup.

Milk & Cereal Consumption	African-American	African Migrant	African Nigerian	Total	p-value
Milk	201 (81.0)	55 (94.8)	487 (76.0)	743 (78.5)	<0.002
Whole milk	94 (46.8)	18 (32.7)	49 (10.1)	161 (21.7)	<0.001
2% milk	60 (29.9)	14 (25.5)	6 (1.2)	80 (10.8)	
1% milk	11 (5.5)	2 (3.6)	1 (.002)	14 (1.9)	
Skim/Non-fat milk	18 (9.0)	4 (7.3)	4 (.008)	26 (3.5)	
Evaporated/Powder	3 (1.5)	8 (14.6)	421 (86.4)	432 (58.1)	
Soy	10 (5.0)	3 (5.5)	0	13 (1.7)	
Non-Dairy creamer	5 (2.5)	0	3 (.006)	8 (1.1)	
Cereal	194 (78.2)	49 (84.5)	287 (44.8)	530 (56.0)	<0.001
Granola	5 (2.6)	4 (8.2)	2 (.006)	11 (2.1)	
High Fiber	54 (27.8)	19 (38.8)	4 (1.4)	77 (14.5)	
Whole grain	44 (22.7)	12 (24.5)	14 (4.9)	70 (13.2)	
Fortified	13 (6.7)	4 (8.2)	2 (.006)	19 (3.6)	
Frosted, Fruit loop	85 (43.8)	14 (28.6)	22 (7.7)	121 (22.8)	
Oat meal	70 (36.1)	9 (18.4)	49 (17.1)	128 (24.2)	
Corn pap	39 (20.1)	6 (12.2)	246 (85.7)	291 (54.9)	

Table 4a: Consumption of selected vegetables and preparation with fats and oils in the last three months by ethnic subgroup.

Vegetables and Oils	African-Americans	African Migrant	African Nigerians	Total	p-value
Yam/Plantain/Squash	152 (61.3)	54 (93.1)	599 (93.4)	805 (85.0)	<0.001
Fried	23 (15.1)	15 (27.8)	155 (25.9)	193 (24.0)	
Often/Always	21 (13.8)	13 (24.1)	104 (17.4)	197 (24.4)	
Fried Sometimes	145 (95.4)	25 (46.3)	278 (46.4)	448 (55.7)	
Rarely/Never Fried					
Usual Frying Oil					<0.001
Stick margarine	12 (7.9)	2 (3.7)	2 (.003)	16 (2.0)	
Tub margarine	5 (3.3)	3 (5.6)	3 (.005)	11 (1.4)	
Butter	13 (8.6)	1 (1.9)	5 (.008)	19 (2.4)	
Shortening	35 (23.0)	2 (3.7)	2 (.003)	39 (4.8)	
Olive/Canola oil	67 (44.1)	16 (29.6)	4 (.006)	87 (10.8)	
Corn oil	11 (7.2)	9 (16.7)	7 (.012)	27 (3.4)	
Peanut/Sunflower	127 (83.6)	20 (37.0)	141 (23.5)	288 (35.8)	
Spray oil	5 (3.3)	1 (1.9)	5 (.008)	11 (1.4)	
Palm oil	19 (12.5)	7 (13.0)	452 (75.5)	478 (59.4)	
Add Fat When Cooking	146 (58.9)	32 (55.2)	519 (81.0)	697 (73.6)	
Add Fat After Coking	36 (14.5)	25 (43.1)	302 (47.1)	363 (38.3)	

Table 4b: Pattern of consumption of fats & oils on breads, muffins etc. in the last three months by ethnic subgroup.

Food Item	African-Americans	African Migrants	African Nigerians	Total	p-value
Fat on Bread etc.					
Stick margarine	49 (19.8)	8 (13.8)	92 (14.4)	149 (15.7)	ns
Tub margarine	22 (8.9)	10 (17.2)	64 (10.0)	96 (10.1)	0.02
Butter	121 (48.8)	12 (20.7)	66 (10.3)	199 (21.0)	0.001
Olive/Veg. oil	3 (1.2)	2 (3.4)	8 (1.2)	13 (1.4)	ns
Palm oil base items	0	0	38 (5.9)	38 (4.0)	<0.001

Table 5: Pattern of consumption of ice cream, yogurt, salad dressing & mayonnaise in the past three months by ethnic subgroup

Food Item	African-Americans	African Migrants	African Nigerians	Total 947	p-value
Ice Cream/Yogurt					<0.001
Regular	169 (68.1)	17 (29.3)	150 (23.4)	336 (35.5)	
Low fat	33 (13.3)	15 (25.9)	22 (3.4)	70 (7.4)	
Fat free	13 (5.2)	8 (13.8)	2 (.003)	23 (2.4)	
None	34 (13.7)	23 (39.7)	467 (72.9)	524 (55.3)	
Salad Dressing					<0.001
Regular	171 (70.0)	20 (34.5)	111 (17.3)	302 (31.9)	
Low fat	38 (15.3)	11 (19.0)	10 (1.6)	59 (6.2)	
Fat free	25 (10.1)	12 (20.7)	3 (.005)	41 (4.3)	
None	18 (7.3)	15 (25.9)	517 (80.7)	550 (58.1)	
Mayonnaise					0.007
Regular	146 (58.9)	16 (27.6)	36 (5.6)	198 (20.9)	
Low fat	32 (12.9)	8 (13.8)	1 (.002)	41 (4.3)	
Fat free	11 (4.4)	3 (5.2)	8 (1.2)	22 (2.3)	
None	60 (24.2)	31 (53.4)	596 (93.0)	687 (72.5)	

Table 6: Pattern of consumption of cookies, crackers, cakes and pastries in the last three months by ethnic group

Food Items	African-Americans	African Migrants	African Nigerians	Total	p-value
Cookies	231 (93.1)	17 (29.3)	467 (72.9)	737 (77.8)	<0.001
Low-fat Crackers					<0.001
Often-Always	51 (22.1)	15 (38.5)	155 (33.2)	221 (29.9)	
Sometimes	67 (29.0)	12 (30.8)	200 (42.8)	279 (37.9)	
Rarely-Never	113 (48.9)	12 (30.8)	112 (24.0)	237 (32.2)	
Cakes / Pastries	225 (90.7)	37 (83.8)	296 (46.2)	558 (58.9)	<0.001
Low-fat Cakes					<0.001
Often-Always	30 (13.4)	6 (16.2)	37 (12.5)	73 (13.1)	
Sometimes	49 (21.8)	15 (40.5)	121 (40.9)	185 (33.2)	
Rarely-Never	146 (64.9)	16 (43.2)	138 (46.7)	300 (53.8)	

Table 7: Pattern of consumption of popcorn in the last three months by ethnic subgroup.

Food Item	African-Americans	African Migrants	African Nigerians	Total	p-value
Popcorn	165 (66.5)	30 (51.7)	207 (32.3)	402 (42.4)	<0.001
Type of Popcorn					
In Oil *	22 (13.3)	5 (16.7)	79 (38.2)	107 (26.6)	<0.001
Regular	124 (75.2)	18 (60.0)	73 (35.3)	215 (53.5)	
Microwave	24 (14.5)	7 (23.3)	56 (27.1)	87 (21.6)	
Air / Special lite					
Add Butter/Fat **					
Often-Always	41 (24.8)	4 (13.3)	48 (23.2)	93 (23.1)	<0.001
Sometimes	7 (4.2)	2 (6.7)	53 (25.6)	62 (15.4)	
Rarely-Never	117 (70.9)	24 (80.0)	106 (51.2)	247 (61.4)	

* Includes popcorn at the movies (Americans only)

** Includes eating popcorn with peanuts, coconuts etc (Nigerians only)

Table 8. Pattern of consumption of corn in the last three months by ethnic subgroup.

Food Item	African-Americans	African Migrant	African Nigerians	Total	p-value
Corn	218 (87.9)	44 (75.9)	476 (74.3)	738 (77.9)	<0.001
Preparation/Form					
Boiled corn	126 (57.8)	33 (75.0)	399 (83.8)	558 (75.6)	<0.001
Roasted corn	22 (10.1)	11 (25.0)	355 (74.6)	388 (52.6)	
Can corn	141 (64.7)	6 (13.6)	7 (1.5)	154 (20.9)	
Corn cake *	0	3 (6.8)	72 (15.1)	75 (10.2)	
With Fat					
No fat added	88 (40.4)	28 (63.6)	262 (55.0)	378 (51.2)	<0.001
Butter/Margarine	128 (58.7)	8 (18.2)	2 (.004)	138 (18.7)	
Peanut/Coconut	1 (.005)	5 (11.4)	203 (42.6)	209 (28.3)	

Table 9: Pattern of corn flour consumption in the last three months by ethnic subgroup.

Food Item	African-Americans	African Migrants	African Nigerians	Total	p-value
Corn Flour	200 (80.6)	35 (60.3)	537 (83.8)	771 (81.4)	<0.001
Corn Flour Form					
Corn Bread	200 (100.0)	13 (37.1)	30 (5.6)	243 (31.5)	<0.001
Corn Pudding *	2 (1.0)	14 (40.0)	393 (73.2)	409 (53.0)	
Fermented Pudding **	0	10 (28.6)	322 (60.0)	332 (43.1)	
Others	1 (0.005)	3 (8.6)	27 (5.0)	31 (4.0)	
With Sauce/Fat					
None	19 (9.5)	0	19 (3.5)	38 (4.9)	<0.001
Beans, Bean cake	10 (5.0)	2 (5.7)	100 (18.6)	112 (14.5)	
Veg oil tomato sauce	17 (8.5)	8 (22.9)	91 (16.9)	116 (15.0)	
Palm oil tomato sauce	5 (2.5)	5 (14.3)	60 (11.2)	70 (9.1)	
Egusi sauce ***	0	2 (5.7)	35 (6.5)	37 (4.8)	
Ogbolo/okra sauce ***	1 (.005)	2 (5.7)	31 (5.8)	34 (4.4)	
Butter	15 (7.5)	2 (5.7)	0	17 (2.2)	
Margarine	5 (2.5)	0	0	5 (.006)	
Beef stew	2 (1.0)	0	0	2 (.003)	
Milk	0	0	2 (.004)	2 (.003)	

* Pap or 'Akamu'

** 'Kenki' / 'Agidi'

*** Nigerian sauce

Table 10: Pattern of rice consumption in the last three months by ethnic subgroup.

Food Item	African-Americans	African Migrants	African Nigerians	Total	p-value
Rice	219 (88.3)	53 (91.4)	618 (96.4)	890 (94.0)	<0.001
Rice preparation					
Plain	3 (1.4)	0	3 (.005)	6 (.008)	<0.001
Butter/Margarine	143 (65.3)	5 (9.4)	10 (1.6)	158 (17.8)	
With Tomato sauce	76 (34.7)	50 (86.2)	598 (96.8)	723 (81.2)	
'Jollof' rice *	5 (2.3)	25 (43.1)	212 (34.3)	242 (27.2)	
Fried rice	20 (9.1)	19 (32.8)	99 (16.0)	138 (15.5)	
Chinese fried rice	22 (10.0)	3 (5.2)	0	25 (2.8)	
With Gravy	15 (6.8)	1 (1.7)	0	16 (1.8)	
Other forms	7 (3.2)	1 (1.7)	4 (.006)	12 (1.3)	

* Spanish style

Table 11: Pattern of pasta consumption in the last three months by ethnic subgroup.

Food Item	African-Americans	African Migrants	African Nigerians	Total	p-value
Spaghetti / Macaroni	210 (84.7)	27 (46.6)	106 (16.3)	343 (36.2)	<0.001
Pasta Preparation					<0.001
With Tomato sauce	152 (72.4)	24 (88.9)	97 (91.5)	273 (79.6)	
With Cheese	93 (44.3)	0	1 (.009)	94 (27.4)	
Butter/Margarine	31 (14.8)	2 (7.4)	15 (14.2)	48 (14.0)	
Lasagna	19 (9.0)	2 (7.4)	3 (2.8)	24 (7.0)	
Pasta salad	4 (1.9)	1 (3.7)	1 (.009)	6 (1.7)	

Table 12: Pattern of hamburger consumption in the last three months by ethnic subgroup.

Food Item	African-Americans	African Migrants	African Nigerians	Total	p-value
Hamburger	216 (87.1)	41 (70.7)	24 (3.7)	281 (29.7)	<0.001
Condiments					<0.001
Cheese	144 (66.7)	14 (34.1)	0	158 (56.2)	
Mayonnaise	142 (65.7)	18 (43.9)	2 (8.3)	162 (57.7)	
Mustard	149 (69.0)	16 (39.0)	0	165 (58.7)	
Tomato ketchup	15 (6.9)	10 (24.4)	0	25 (8.9)	
French fries	137 (63.4)	23 (56.1)	2 (8.3)	162 (57.7)	
Sliced Tomato	169 (78.2)	23 (56.1)	7 (29.2)	199 (70.8)	
Lettuce	168 (77.8)	23 (56.1)	3 (12.5)	194 (69.0)	
Pickle	164 (75.9)	20 (48.8)	8 (33.3)	192 (68.3)	
Others *	70 (32.4)	8 (19.5)	4 (16.7)	82 (29.2)	

* Onion etc.

Table 13: Pattern of consumption of fried seafood in the last three months by ethnic subgroup.

Food Item	African-Americans	African Migrants	African Nigerians	Total	p-value
Fried Seafood					<0.001
Fried in batter (crust)	173 (69.8)	17 (29.3)	21 (3.3)	211 (22.3)	
Fried Plain	28 (11.3)	27 (46.6)	373 (58.2)	428 (45.2)	
Not fried *	85 (34.3)	17 (29.3)	213 (33.2)	315 (33.3)	
No Response **	6 (2.4)	7 (12.1)	124 (19.3)	137 (14.5)	

*Broiled/Baked

** Did not eat seafood

APPENDIX C:

Abstract 1: Abstract accepted and presented at IMPaCT meeting, March 2007.
Innovative Minds in Prostate Cancer Today: Program page 22.

Dietary Fat and Prostate Cancer Risk among African-Americans and Africans:

A Case-Control Study.

Flora A.M. Ukoli; Abu K. Taher; Emeka Amaefuna; Phillip Akumabor (University of Benin, Nigeria); Usifo Osime (University of Benin, Nigeria); Lucille Adams-Campbell (Howard University, Washington DC); and Derrick Beech.

Although genetic predisposition has been suggested as one of the reasons for high prostate cancer (PCa) incidence among African-Americans, exposure to dietary cancer promoting factors such as saturated fats and Omega-6 fatty-acids may also be very important. Autopsy studies reported that Africans who are genetically related to African-Americans record lower rates of aggressive disease, even though they have similar rates of latent disease. Using funds from the Department of Defense Prostate Cancer Research Program Fiscal Year 2005, we studied the eating pattern, body fat distribution, and fatty-acid profile of African-American and African men in Washington DC and Nashville metropolitan areas, and four communities in southern Nigeria. Cases identified through the state cancer registries were invited by mail, telephone, and flyers displayed in urology offices. Community controls were recruited by flyers distributed in doctors' offices, churches, health centers, door-to-door (Nigeria), and newspaper, radio and television announcements. Free PCa screening events also served as recruitment opportunities. PSA was analyzed by a commercial laboratory and fatty-acids by a specialized research laboratory. Of 848 consented participants, 218(25.7%) were African-Americans, 66(7.8%) African Migrants, and 564(66.5%) were Nigerians. The mean ages for the 516 men with fatty-acid profile information were 57.1(9.7), 53.0(8.5), and 60.7(13.8) respectively, $p < 0.0001$. There were 59(11.5%) cases, 256(49.6%) controls, and 201(38.9%) with elevated PSA and/or enlarged prostate. Mean differences across ethno-cultural groups for Omega-6 (Arachidonic, Linoelic, Adrenic, Docosapentaenoic, Dihomo-g-Linolenic), Omega-3 (Eicosapentaenoic (EPA), Docosahexaenoic (DHA), Alpha-Linolenic), and selected physiologically relevant fatty-acids (Palmitic, Stearic, Oleic) were significant, $p < 0.011 - p < 0.0001$, except for Vaccenic acid (C18:1). The proportion of variance due to ethnic group was 42.4% and 42.6% for total Omega-6 and total Trans fatty-acids respectively, and 19.7% for Omega-3 fatty-acid Alpha-Linolenic. African-Americans recorded the highest mean total Omega-6 fatty-acids [1132.80(264.7)], followed by African migrants [1077.86(233.4)], and Nigerians [694.52(209.1)], $p < 0.0001$. Mean Omega-3 index was respectively 2.34(1.2), 4.12(1.8), and 3.88(1.9), $p < 0.0001$. PCa cases had higher mean Omega-6 fatty acid, $p < 0.07$, odds ratio for PCa risk was 3.4 (95%CI 2.4 – 4.4) between the upper and lower quartile. The BMI for African-Americans, African migrants and Nigerians was 28.6(6.1), 28.5(4.0), and 23(4.0) respectively. 6.1% African-Americans recorded Omega-3 index $\geq 8\%$, compared to 37.9% and 36.9% for African migrants and Nigerians.

IMPACT: Exposure to higher levels of dietary Omega-6 fatty-acids may explain some of the excess PCa risk among African-Americans in comparison to their genetic relatives in Nigeria. African migrants have similar BMI as African-Americans, but they record high mean Omega-3 index as their peers in Nigeria, with whom they share a similar diet high in Omega-3 fatty-acids. There is need to recruit more cases to allow for statistically adequate within group analysis. These preliminary findings warrant a need to evaluate the dietary styles of the three sub-populations to inform dietary style patterns that may control dietary fatty-acid PCa risk across black populations. Improving the Omega-3 index is particular urgent for cardio-protection as well as PCa risk reduction.

Abstract 2: Abstract accepted and presented at AORTIC, 2007. South Africa.
AORTIC 2007 OAREC. Page 86.

Paper Title: Dietary Fatty Acids and Prostate Cancer Risk among Nigerians: A Case-Control Study.

Authors: **Flora A.M. Ukoli**¹, Khandaker A. Taher¹, Emeka Amaefuna¹, Jay Fowke², Harvey Murff², Usifo Osime³, Phillip Akumabor³, Derrick Beech¹.

Authors' affiliations: 1: Meharry Medical College, Nashville, TN. U.S.A.
2: Vanderbilt University, Nashville, TN. U.S.A.
3: University of Benin, Benin-City, Edo State, Nigeria.

Corresponding author's email: fukoli@mmc.edu

Introduction: Increased incidence of prostate cancer (PCa) in Nigeria is explained by aging population and improved diagnosis. We explored the role of fatty acids (FAs) in PCa risk.

Materials and methods: Men 40 years and older at urology and surgical clinics of University of Benin Teaching Hospital 256(42.2%), and from the community 350(57.9%) were recruited. Urologic symptom history was collected, digital rectal examination (DRE) performed, fasting blood collected, and prostate specific antigen (PSA) measured. Men with abnormal DRE and/or PSA were reviewed and managed by the urologist. Plasma FAs were analyzed using gas liquid chromatography, and completed for 340 of 606 participants, 66(19.4%) cases, 226(66.5%) controls, and 48(14.1%) with PSA \geq 4ng/ml.

Results: Mean age for cases and controls was 71.91 \pm 11.47 and 56.65 \pm 12.69, $p < 0.0001$. 63.0% had less than secondary education, 73.4% married, 60.3% employed, and 88.8% in the lowest income third. Median total, omega-6, and saturated FA were higher among cases (2,447ug/ml to 2,374ug/ml, 694ug/ml to 654ug/ml $p < 0.06$, and 887ug/ml to 846ug/ml respectively), and omega-3 was insignificantly lower (97ug/ml to 105ug/ml). Adjusted odds ratios for PCa risk were 2.18(95%CI 0.54-8.81) and 1.04(95%CI 0.41-2.64) for omega-6 and omega-3 FAs, significant for nervonic and arachidonic acids, 2.36(95%CI 1.06-5.22) and 1.70(95%CI 1.04-7.56) respectively.

Conclusions: Nervonic and arachidonic acids appear to be associated with increased PCa risk. These findings should be confirmed in larger studies and dietary patterns predisposing to unfavorable FA profiles investigated in this population. Further research is required to better understand interactions between various FAs and other nutrients in PCa risk.

Abstract 3: Poster presentation at AORTIC, Oct. 2007.

Book of Abstracts: AORTIC 2007 OAREC. Page 186 – 187.

A comparative evaluation of the fatty acid profiles of African-Americans and Africans: Implications for prostate cancer risk.

Khandaker A. Taher¹, Temple Oguike², Usifo Osime², Jay H. Fowke³, Harvey J. Murff³, Derrick J. Beech¹, Flora A. M. Ukoli¹

¹Departemnt of Surgery, Meharry Medical College, Nashville, TN

²University of Benin, Benin-City, Edo State, Nigeria

³ Department of Medicine, Vanderbilt University School of Medicine, Nashville, TN

OBJECTIVE: Prostate cancer (PCa) incidence for African-Americans is five times that of Africans with similar latent PCa rates at autopsy. Fatty acids (FAs) from animal sources are incriminated in PCa risk. We compare the FA profiles of these two populations to elucidate implications for PCa risk disparity.

METHODS: A total of 458 participants, Nigerians (N=311) from the community and urology clinics, University of Benin Teaching Hospital, and African-Americans (N=147) from the community and cancer registry, comprising 53(17.0%) and 27(18.4%) PCa cases respectively, provided demographic, urology symptom data, and fasting blood for PSA and FA profile.

RESULTS: Mean age of Nigerians compared to African-Americans was 60.7±13.8 to 57.1±9.7, $p<0.001$. Median total, omega-6, and trans FAs were lower among Nigerians (2,439µg/ml to 2,654ug/ml, $p<0.0001$; 666µg/ml to 1,103µg/ml, $p<0.0001$; and 17µg/ml to 72µg/ml, $p<0.0001$ respectively), while omega-3 and ω-9 FAs were higher (101µg/ml. to 85µg/ml, $p<0.0001$ and 625µg/ml to 522µg/ml, $p<0.0001$, respectively). Among African-Americans less than secondary education predicted high saturated FA, (OR 3.8; 95%CI 1.2-12.0) while total, omega-6 and omega-3 FAs were not predicted by demographic variables. Age <55years significantly predicted total FA among Nigerians (OR 0.29; 95%CI 0.09 – 0.95), and significant predictors of omega-6 FA were age (OR 0.27; 95%CI 0.07-0.97) and less than primary education, (OR 0.23; 95%CI 0.09 – 0.60).

CONCLUSIONS: Significant differences exist in the FA profile of both populations, Nigerians recording lower omega-6 and higher omega-3 that may explain their lower PCa risk. The dietary and genetic basis for these FA profile differences need to be further studied.

Keywords: Nigerians, African-Americans, Prostate cancer

Abstract 4: Poster presented at AACR, November 27-30, 2007. Atlanta GA.
The Science of Cancer Health Disparities in Racial/Ethnic Minorities and the Medically Underserved.
Program and Proceedings: Poster Session A51. Page 56.

Title: A comparative study of serum linoleic acid in prostate cancer risk between African-Americans and Africans.

Authors: **Khandaker A. Taher**¹, Rodney Davis¹, Carlton Z. Adams¹, Philip Akumabor², Usifo Osime², Flora A.M. Ukoli¹

Authors' affiliations: 1: Meharry Medical College, Nashville, TN. U.S.A.
2: University of Benin, Benin-City, Edo State, Nigeria.

Corresponding author's address & email: 1005 Dr. D. B. Todd blvd.
Nashville, TN 37208
ktaher@mmc.edu

Introduction: There is some evidence that higher dietary intake and blood level of linoleic acid are associated with a reduced risk of prostate cancer but findings have been conflicting. Prostate cancer incidence rate for African-Americans is five times that of African-Nigerians with similar rates found at autopsy. We compared the serum linoleic acid (C18:2) levels to elucidate the prostate cancer risk disparity between these two populations.

Methods: A case-control study was conducted among 458 men, Nigerians (N=311) from the community and urology clinics at University of Benin Teaching Hospital, and African-Americans (N=147) who provided fasting blood samples. Quantitative measurement of serum linoleic acid levels and other abundant fatty acids were done using capillary gas chromatography. Conditional logistic regression was used to compute adjusted odds ratios (ORs) and 95% confidence intervals (95% CI) of prostate cancer in the highest quartile of serum linolenic acid ($\mu\text{g/ml}$) level in relation to the lowest quartile for each population.

Results: Mean age of Nigerians compared to African-Americans was 60.7 ± 13.8 to 57.1 ± 9.7 , $p < 0.001$. Among Nigerian median total fatty acids and n-6 fatty acids were lower ($2,439 \mu\text{g/ml}$ to $2,654 \mu\text{g/ml}$, $p < 0.0001$; $666 \mu\text{g/ml}$ to $1,103 \mu\text{g/ml}$, $p < 0.0001$ respectively), while n-3 fatty acids were higher ($101 \mu\text{g/ml}$ to $85 \mu\text{g/ml}$, $p < 0.0001$) in comparison to African-Americans. Serum linoleic acid was inversely related to overall prostate cancer risk ($\text{OR}_{\text{Q4vs.Q1}}$, 0.32; 95%CI, 0.11-0.96; $P_{\text{trend}} = 0.04$ among African-Americans and was not related to prostate cancer risk ($\text{OR}_{\text{Q4vs.Q1}}$, 4.00; 95%CI, 0.98-16.42; $P_{\text{trend}} = 0.20$) among Nigerians.

Conclusions: Our study suggests that there are some significant differences exist in the fatty acids profiles between African-Americans and Nigerians. The comparatively low incidence of prostate cancer in Nigeria may be related to the lower n-6 and higher n-3 fatty acids levels in blood. The apparent protective effective of serum linoleic acid was found for African-Americans but not consistent for Nigerians. The direct association of linoleic acid metabolites with prostate cancer risk are needed to be further investigated in these disparate populations.

Keywords: Nigerians, African-Americans, Prostate cancer

Abstract 5: Abstract in preparation for submission in 2008.

Omega-6:Omega-3 Ratios in Prostate Cancer Risk among Men of African Descent: A Case-Control Study.

Authors: **Flora A.M. Ukoli**¹, Khandaker A. Taher¹, Carlton Adams, Jr.¹, Harvey Murff², Temple Oguike³, Derrick Beech¹.

Introduction:

Exposure to a high-fat diet may be more important than genetic predisposition in the etiology of prostate cancer among African-Americans, who continue to record the highest incidence rates in the world. Essential (LA) and non-essential (AA) omega-6 and essential (ALA) omega-3 fatty-acids are reported to be associated with increased risk for prostate cancer, while non-essential marine omega-3 fatty acids are associated with reduced risk in epidemiological studies. It has also been demonstrated that these fatty acids respectively promote and inhibit prostate cancer cell-growth in vitro. Essential fatty acids are derived from dietary intake and are not synthesized in the body while non-essential fatty acids are derived from dietary sources as well as metabolized in vivo from the same group essential fatty acid. AA and DGLA are metabolites of LA, the later can also be converted to prostaglandins that are favorable for prostate health. EPA and DHA are metabolites of ALA, both of which are metabolized to favorable prostaglandins. It has therefore been proposed that striking a healthy omega-6:omega-3 balance in the diet can be useful in controlling prostate cancer initiation and promotion. Sub-Saharan Africa, a designated prostate cancer low-incidence region, now experiences increasing rates of prostate cancer. This trend is attributed to increased diagnosis and a shift towards a Westernized diet with unfavorably high omega-6:omega-3 ratio, among other factors. Men in this region tend to be lean and traditionally eat a high-carbohydrate-low-fat diet. This study investigates the combined role of omega-6 and omega-3 fatty acids in prostate cancer risk across culturally diverse populations of common African ancestry, with very different dietary styles.

Materials and Methods: The eating pattern, body fat distribution, and fatty-acid profile of African-Americans in Washington DC and Nashville metropolitan areas, and Africans from four communities in southern Nigeria was collected. Prostate cancer cases identified through the state cancer registries were invited by mail, telephone, and by flyers displayed in urology offices. Community controls were recruited by flyers distributed in doctors' offices, churches, health centers, door-to-door (Nigeria), and through newspaper, radio and television announcements. Free prostate cancer screening events at health fairs also served as recruitment opportunities. PSA was analyzed by a commercial laboratory and fatty-acids measured by gas chromatography in a specialized research laboratory. The fatty acid ratios considered included omega-6:omega-3, essential:non-essential omega-6, essential:non-essential omega-3, and arachidonic:marine omega-3. Of 848 consented participants, 218(25.7%) African-Americans, 66(7.8%) African Migrants, and 564(66.5%) Nigerians, fatty acid analysis was completed for all cases and selected controls. The respective mean ages for the 516 men with fatty-acid profile information are 57.1(9.7), 53.0(8.5), and 60.7(13.8) respectively, $p < 0.0001$. The association between four categories of fatty acid ratios and prostate cancer risk was calculated separately for African-Americans and Nigerians, first by comparing median ratios between cases and controls using the Mann-Whitney non-parametric test, and by estimating association of as measured by odds ratio using multiple regression controlling for

body fat measures and selected demographic characteristics.

Results: There were 59(11.5%) cases, 256(49.6%) controls, and 201(38.9%) with elevated PSA and/or enlarged prostate. African-Americans recorded higher ω -6: ω -3 ratios, lower LA:AA ratio, lower omega-3 indices, and higher AA:marine w-3 ratios, $p < 0.0001$. Cases recorded lower LA:AA ratios in both populations, while w-6:3 ratios, AA:marine w-3, and ALA:EPA were higher, and omega-3 indices were lower only among Nigerian cases. Mean Omega-3 index was respectively 2.34(1.2), 4.12(1.8), and 3.88(1.9), $p < 0.0001$. PCa cases had higher mean Omega-6 fatty acid, $p < 0.07$, odds ratio for PCa risk was 3.4 (95%CI 2.4 – 4.4) between the upper and lower quartile. The BMI for African-Americans, African migrants and Nigerians was 28.6(6.1), 28.5(4.0), and 23(4.0) respectively. 6.1% African-Americans recorded Omega-3 index $\geq 8\%$, compared to 37.9% and 36.9% for African migrants and Nigerians.

Conclusion: Exposure to higher levels of dietary Omega-6 fatty-acids may explain some of the excess PCa risk among African-Americans in comparison to their genetic relatives in Nigeria. African migrants have similar BMI as African-Americans, but they record high mean Omega-3 index as their peers in Nigeria, with whom they share a similar diet high in Omega-3 fatty-acids. There is need to recruit more cases to allow for statistically adequate within group analysis. These preliminary findings warrant a need to evaluate the dietary styles of the three sub-populations to inform dietary style patterns that may control dietary fatty-acid PCa risk across black populations. Improving the Omega-3 index is particular urgent for cardio-protection as well as PCa risk reduction.

APPENDIX D: Publications:

List of Publications:

1. Flora A. Ukoli, Eruke Egbagbe, Barbara B. Zhao, Efosa Iyamu, Dale Young, Philip Osime, Usifo Osime, Lucile L. Adams-Campbell. Anthropometric Body Fat Predictors of Elevated Prostate Specific Antigen among Rural and Urban Nigerians: A Population-Based Study. WJMJ. 2007; 26(1):7-13.
2. F.A. Ukoli, E. Egbagbe, F. Akereyeni, E. Iyamu, T. Oguike, P. Akumabor, and U. Osime. Response to Prostate Biopsy by Nigerian men: Community and Hospital Experience. Proceedings of the UICC World Cancer Congress, Washington D.C.(USA), July 8-12. 2006. Pgs 341- 347. Medimond. International Proceedings.
3. F. Ukoli, U. Osime, F. Akereyeni, O. Okunzuwa, R. Kittles, L. Adams-Campbell. Prevalence of Elevated Serum Prostate Specific Antigen in Rural Nigeria. International Journal of Urology. 2003; 10:315-322.

Manuscripts under preparation:

1. Plasma fatty acids and prostate cancer risk among African-Americans and Africans.
2. A comparative study of serum linoleic acid in prostate cancer risk among African-Americans and Africans.

The association of plasma fatty acids with prostate cancer risk in African-Americans and Africans.

Ukoli, FA¹, Taher, KA¹, Amaefuna E¹, Akumabor P², Osime U^{2, 1}

¹ Meharry Medical College, Nashville, TN

² University of Benin, Nigeria

Address correspondence to Dr. K. A. Taher, Department of Surgery, Meharry Medical College, 1005 Dr.D.B.Todd Jr. Blvd., Nashville, TN 37208. E-mail: fukoli@mmc.edu

ABSTRACT

Background: African-American ethnicity and subSaharan African ancestry have been recognized as a risk factor for prostate cancer. Animal and *in-vitro* studies have reported significant associations of fatty acids with prostate cancer but epidemiological studies remain unclear.

Methods: 458 men were recruited in an ongoing case-control study of dietary fat and antioxidant in prostate cancer risk among African-Americans and West Africans for the quantitative determination of C8-C26 total fatty acids in plasma by GC/MS methods. We estimate the prostate cancer risk in the highest quartile of plasma fatty acid ($\mu\text{g/ml}$) level in relation to the lowest quartile for each population.

Results: A total of saturated, n-9 and n-3 fatty acids were higher among Nigerians, while a total of both *trans* and n-6 fatty acids were higher among African Americans. All individual fatty acids were found significantly different in both populations except for vaccenic and mead acid which remained equivocal. Our data failed to demonstrate any relationship of total n-3, n-5, n-6, and n-7 with PCa risk among neither population. Among African-Americans a total *trans* fatty acids exerts significant risk ($P_{\text{trend}} < 0.05$) while adjusted ORs increased across the gradient but findings were not significant ($P_{\text{trend}} = 0.11$). The total *trans* contributes twice more risk in disease causations among African-Americans than Nigerians. It was found significant risk factor for prostate cancer among African-Americans those have higher levels of total trans fatty acids (OR, 4.09; 95% CI 0.28-59.59 $P_{\text{trend}} = 0.02$). Among African-Americans myristic acid was found protective (OR, 0.70; 95% CI 0.20-2.42, $P_{\text{trend}} = 0.03$). Behenic acid (OR, 2.42; 95% CI 0.95-6.15, $P_{\text{trend}} = 0.01$) among Nigerians and Erucic acid (OR, 3.96; 95% CI 1.05-14.90 $P_{\text{trend}} = 0.05$) appeared to be risk factor.

Conclusions: There were significant differences in the total plasma concentrations of all fatty acids, saturated, n-9, n-6, n-3, and *trans* fatty acids exist between African-Americans and Nigerians. These differences also retained in all individual fatty acids except for vaccenic and mead acids.

INTRODUCTION

African-American men have consistently recorded the highest reported prostate cancer incidence rates in the world over many decades (1). African-American ethnicity has been recognized as significant risk factor for developing prostate cancer (2). Along with increasing age and a positive family history subSaharan African ancestry has also been recognized as an important risk factor for prostate cancer (3). The recorded incidence of prostate cancer varies enormously around the world. The global data of directly age-standardized incidence (using the World standardized population) has designated Nigeria as a country of intermediate-incidence region of less than 24.5 per 100,000 (4). Despite the absence of screening programs in Nigeria, the number of prostate cancer cases has been increasing. Current incidence rate in Nigeria was found much higher than ever reported previously (5) (6). In comparative studies done long before PSA era in Washington, D.C., and Ibadan, Nigeria, the incidence of latent prostate cancer was the same, although there was a 10-fold difference in the clinical prostate cancer rate (7). Another comparative study between healthy indigenous Africans and African-Americans revealed the differences of levels of estrogen and androgen metabolites and urinary steroids depend on their respective diets (8). Because the growth and differentiation of the prostate is under androgen control and men with congenital abnormalities in androgen metabolism do not develop prostate cancer, yet hormonal factors remain as risk for prostate cancer (9). Therefore, diet appears to be more attributable to the disparate clinical prostate cancer incidence rates with a variable magnitude between these two populations.

A possible ecological link between prostate cancer and diet was originally suggested based on international differences in mortality rates and national average intakes of fats (10). In a multicenter study of dietary factors, prostate cancer risk was associated with total fat intake in whites, African-Americans and Asian Americans (11). About 10% to 15% of the difference in prostate cancer incidence among these ethnicities has been estimated to account for differences in saturated fat intake. Other studies have linked consumption of diets rich in red meats with prostate cancer risk (12) (13). The study linked greater consumption of fat from animal sources to increased risk of prostate cancer among African-Americans also showed that a reduction of fat from animal sources in the diet could lead to decreased incidence and mortality for prostate cancer, particularly among African-Americans (14). Unlike western diet predominantly rich in fats, Nigerians living on a traditional diet with high fish content but less meat, lower animal fat may be attributed to the relative low incidence of prostate cancer than their counterpart (6).

Biological markers are believed to be more objective than food frequency questionnaires (FFQs), because biomarkers do not rely on the precision of food composition databases and self-reports or the appropriateness of FFQ items (15). Most case-control studies have associated high intakes of animal fat or saturated fatty acids with an increased risk of prostate cancer using food-frequency questionnaires, but only a few of them have an appropriate biomarker (16). The fatty acid (FA) composition of plasma lipids reflects the type of dietary fat and has been used as an objective estimate of the type of fats proportionally consumed by an individual (17),(18). Even plasma phospholipid fatty acid composition was used as a biomarker of habitual dietary fat intake in an ethnically

diverse cohort (19). Therefore, fasting plasma has also been suggested as a suitable biomarker of essential fatty acids intake in many epidemiologic studies (20). We examined associations between different plasma fatty acid concentrations and prostate cancer risk among African-Americans and Nigerians.

Materials and Methods

Study Population

Participants were 458 men recruited in an ongoing case-control study of dietary fat and antioxidant in prostate cancer risk among African-Americans and West Africans. All subjects gave informed consent on forms approved by the Ethics Committee of the Meharry Medical College and University of Benin, Nigeria. The African-Americans (N=147) residing in Washington and Nashville metropolitan areas while a subset-set of the West-Africans residing in Nigeria (N=311) were participated. Controls were recruited in Nigeria from churches, mosques, social, and recreational clubs in four selected communities from both urban and rural areas. House to house invitations were offered. Interested persons visited local health center to complete consent form and then returned next day without breakfast for blood draw. Cases were recruited from University of Benin Teaching Hospital in Nigeria. Suitable African-American controls were selected from those who participated in the prostate cancer screening program in Washington and Nashville areas. As for the African-Americans cases, those who were diagnosed prostate cancer with a biopsy confirmation not more than five years ago, were recruited into the

study. After securing the physician's approval, we obtained the informed consent and scheduled a study appointment as soon as possible before treatment starts. Participants were instructed to eat their dinner before 9:00 PM the previous night and to avoid any other foods or drinks until their blood has been drawn.

Data collection

We collected information about sociodemographic characteristics, dietary intake and medical history. Anthropometric measurements were gathered by trained field-workers from subjects wearing light clothing and no shoes. A 30 ml of fasting venous blood were drawn by trained phlebotomists. Samples were centrifuged and plasma was store at -70°C before one microvial of plasmas was sent out for lipid analyses. We sent out samples (Kennedy Krieger Institute, Peroxismal Diseases Laboratory, 707 North Broadway, Baltimore, MD 21205 USA) and a capillary gas chromatography-electron-capture negative-ion mass spectrometry (GC/MS) methods (21) were used for the quantitative determination of C8-C26 total fatty acids in plasma. After addition of the internal standard mixture to 100 µL of plasma, fatty acids were hydrolyzed from triglycerides and phospholipids. Following hydrolysis, hexane extraction, and derivatization with pentafluorobenzyl bromide, resulting fatty acid pentafluorobenzyl esters were dissolved in hexane, then analyzed in two steps: a splitless injection and a second, split injection (1:100) for the quantitation of the more abundant fatty acids. This method reported to be better than gas chromatographic analysis with flame ionization detection (GC/FID) (21).

Data analysis included student t-tests, chi-squared tests, non-parametric tests as appropriate. Conditional logistic regressions were used to estimate the odds ratios (ORs) and 95% confidence intervals (95% CI) of prostate cancer risk in the highest quartile of plasma fatty acid ($\mu\text{g/ml}$) level in relation to the lowest quartile for each population.

RESULTS

Mean ages of Nigerians and African-Americans were 60.7 ± 13.8 , 57.1 ± 9.7 respectively ($p < 0.001$). Age groups between 55 and 64 years were found significantly related to the prostate cancer risk for both populations. Family history of prostate cancer, college and or post-graduate education, moderate socio-economic status were found significantly related to the risk among African-Americans but not among Nigerians (Table 1). Median total fatty acids were found significantly higher in African-American than Nigerians. A total of saturated, n-9 and n-3 fatty acids were significantly higher among Nigerians, while a total of both *trans* and n-6 fatty acids were significantly higher among African Americans. All individual fatty acids were significantly different in both populations except for vaccinic acid (a monounsaturated fatty acid 18:1) and mead acid (a polyunsaturated fatty acid 20:3; n-9) which remain equivocal between two populations (Table 2).

After adjustment for age, levels of education, family history of prostate cancer, and waist-hip ratio, we assessed the risk of prostate cancer based on cumulative fatty acids profiles comparing lowest quartiles with highest quartiles. The adjusted ORs of total fatty acids across the quartiles were not related to the risk among neither population. Although an apparent increment in adjusted OR was observed for both populations but it was not significant. The adjusted ORs of total n-9 fatty acids significantly increased across the quartiles among African-Americans ($P_{\text{trend}} < 0.05$) (Table 3). Unadjusted ORs for total n-9 fatty acids were significantly increased across the gradient ($P_{\text{trend}} = 0.01$) among African-Americans but not for Nigerians (data were not shown here). The similar finding was not observed in Nigerians. A total of n-3, n-5, n-6, and n-7 fatty acids remained unrelated to the risk for these two populations. Among African-Americans a total *trans* fatty acids exerts significant risk ($P_{\text{trend}} < 0.05$) while adjusted ORs increased across the gradient but findings were not significant ($P_{\text{trend}} = 0.11$) (Table 3). The adjusted $OR_{Q4\text{vs}Q1}$, 4.09; 95%CI, 0.28-59.59 among African-Americans and adjusted $OR_{Q4\text{vs}Q1}$, 1.52; 95%CI, 0.50-4.65 among Nigerians were found in the same direction appeared to be a risk factor (Table 3). Unadjusted ORs for total *trans* fatty acids were significantly increased across the gradient ($P_{\text{trend}} < 0.001$) among African-Americans but not for Nigerians (data were not shown here).

Although the adjusted OR for total *trans* fatty acids remained in the same direction indicating probable risk for both populations. The total *trans* contribute twice more risk is disease causations among African-Americans than Nigerians. Meanwhile the median

levels of total *trans* fatty acids was four times higher among African-Americans than Nigerians. It was found significant risk factor for prostate cancer among African-Americans those have higher levels of total trans fatty acids (OR 4.09 95%CI 0.28-59.59 $P_{\text{trend}}=0.02$). Even unadjusted values also indicated the same significant trend among African-Americans. Although the risk was increasing across the quartile gradients but was not statistically significant. (OR 1.52 ;95%CI 0.50-4.65 $P_{\text{trend}}=0.11$). When we explored two important ingredients of *trans* fatty acids; palmitelaidic acid (C16:1 n-9 *trans*) and elaidic acid (C18:1 n-9 *trans*), we found neither became a risk for both populations (Table 4). The total plasma levels of saturated fatty acid exhibited almost same risk for both populations although magnitudes were not more pronounced. The total fatty acids and total n-6 fatty acids demonstrated opposite effects in these two populations. While among African-Americans they are appeared to be risk but for Nigerians they appeared to be protective. Interestingly the total plasma levels of n-3 fatty acids remained as protective in nature for both populations (Table 3). Total plasma levels of n-5, n-7, & n-9 did not appeared to be risk for both populations. Wide significant variations have been observed in the total plasma levels of n-3, n-6, & n-9 fatty acids between two populations except for total n-5 & n-7 fatty acids.

We have measured total 54 individual fatty acids in plasma ranging from C10:0 to C22:6. But we are reporting only 21 physiologically important individual fatty acids [Table 4]. At the level of individual plasma fatty acid we compared between highest and lowest quartiles. Nigerians have four times higher lauric acid (C12:0) than African-Americans. Nigerians have significantly higher plasma levels of Myristic acid (C14:0) than African-

Americans. Among African-Americans myristic acid was found protective (OR, 0.70;95% CI 0.20-2.42, $P_{\text{trend}}=0.03$) similar findings were not observed among Nigerians. Palmitic acid (C16:0), palmitoleic acid (C16:1) and oleic acid (C18:1) were significantly higher among Nigerians but were not related to prostate cancer risk. African-Americans have higher stearic acid (C18:0) although its role in prostate cancer risk was not significant. Behenic acid (C22:0) appeared to be risk factor for prostate cancer among Nigerians (OR, 2.42;95% CI 0.95-6.15, $P_{\text{trend}}=0.01$). Similar finding was not observed among African-Americans. Although median levels of vaccenic acid (C18:1) between two populations were equivocal but it exerted little risk among African-Americans in both adjusted and unadjusted data. Similar findings were not observed among Nigerians. Nervonic acid (C24:1) was significantly higher among Nigerians than African-Americans and also resulted as a apparent risk factor for Nigerians but not for African-Americans. Erucic acid (C18:1) became a risk for African-Americans (OR, 3.96; 95% CI 1.05-14.90 $P_{\text{trend}}=0.05$). Mead acid (C20:3) remains unrelated to prostate cancer risk for both populations while there was no difference exist in the median values.

The median plasma level of essential polyunsaturated linoleic acid (C18:2) was significantly higher among African-Americans than Nigerians. When we compared unadjusted ORs across the quartiles it appeared not to be a risk for African-Americans ($P_{\text{trend}} < 0.05$; data were not shown). After adjustment it also appeared not to be risk factor for both populations although findings were not statistically significant. Its two metabolic products γ -linolenic acid (C18:3) and Dihomo- γ -linolenic acid (C20:3) were significantly higher among African-Americans than Nigerians but were not related to the risk for both

populations. The similar findings were not observed for another metabolite arachidonic acid (C20:4). The median plasma value of arachidonic acid was significantly higher among African-Americans but it appeared not be risk for African-Americans ($P_{\text{trend}} < 0.05$) and for Nigerians ($P_{\text{trend}} = 0.05$). (Table 4)

The median plasma level of other essential polyunsaturated α -linolenic acid (C18:3) was more than two times higher among African-Americans than Nigerians but it was not related to prostate cancer risk for both populations. But its metabolic products, eicosapentaenoic (C20:5), docosapentaenoic (C22:5), and docosahexaenoic (C22:6) acids were not uniformly higher among African-Americans than Nigerians. These three fatty acids were also remaining unrelated to prostate cancer risk for both populations. (Table 4)

DISCUSSION

The incidence of prostate cancer changes in migrants and vary dramatically in ethnically similar populations residing in different geographic locations for example African-American and Nigerians or elsewhere in sub-Saharan countries strongly indicate the environmental factors can greatly influence the risk of this cancer than genetic factors (22). Among environmental factors, fat has been the focus of dietary studies of prostate cancer more than any other dietary component and early epidemiologic studies consistently suggested a possible causal association (23). Although the exact role of fat in the development of prostate cancer is not yet determined precisely, tumor growth and metastasis have both been shown to be substantially affected by specific fatty acids in

many animal and tissue culture model system. A number of fatty acids have been shown to affect several physiologic and cellular processes that could influence, either positively or negatively, the development of prostate cancer (16). Higher consumption of fat and meat, the two main contributors to western diet, has been associated with higher risk of prostate cancers in some epidemiologic studies (24). The African-American reportedly have a diet richer in animal fat than their counterpart white Americans suggesting the role of animal fat in prostate cancer pathogenesis (25). On the other hand, traditional diet with high fish content and low animal fat, as described in Nigeria, is progressively replaced by a western diet containing high animal fat. “Westernization” of lifestyles in Japanese population in 1980s reportedly related to the transition of low incidence to an increased incidence of prostate cancer (26). We found that African-Americans (2,597.94 µg/ml) have statistically higher median total fatty acids than that of Nigerians (2,419.95 µg/ml) although differences were not too wide and were not associated with overall prostate cancer risk among African-Americans and Nigerians [Table 3]. Therefore; gradual westernization of Nigerian diets might have partial contributions in increasing cases of prostate cancer in Nigeria. These findings agree with the finding of the diet of African-Americans is characterized as high in fat and salt and low in fruits and vegetables (27). The fact of the percentage of energy derived from fat varied widely in both populations might reflect on the differences of plasma levels of total fatty acids. National Health and Nutrition Examination Survey (NHANES III) revealed that the percentage of kilocalories from fat was 34% (28). Whereas the majority of available data indicate that 20%-25% of kilocalories in both rural and urban diets is supplied by fat in West African countries particularly in Nigeria (29) (30). The disparate body fat levels also between two

populations was reported earlier where mean percentages of body fat for Nigerians was 11% and for US blacks was 25% (31). Disproportionately higher rate of prostate cancer in African-Americans than Nigerians may be linked to greater consumption of fat from animal sources by African-Americans (14).

The fatty acid composition of plasma lipids and adipose tissue usually reflects the type of dietary fat and may be used as an objective estimate of the type of fats proportionally consumed by an individual (32). Although there are nondietary factors, such as absorption, metabolism and genetic and lifestyle determinants, can affect fatty acid concentrations in human tissues (33), the fatty acid compositions in plasma phospholipids and cholesterol esters reflects medium-term (weeks to months) dietary intake (32). Because blood drawing is more acceptable to study participants than adipose tissue aspiration, fatty acid measurement in plasma lipids appeared to be more feasible in large-scale epidemiological studies (34). In our study, we did not separate the different fractions of plasma: cholesterol ester, phospholipids, and triacylglycerols. Analysis of each fraction is complex and time consuming; thus these fractions are more prone to increased measurement error. We believe that a more detailed subfraction analysis would be less affordable in a large scale epidemiologic study where there is always a trade-off between precision and budget constraints.

It has been reported that serum levels of omega-3 poly unsaturated fatty acids (PUFAs) were significantly lower in patients with benign prostate hyperplasia and prostate cancer, and omega-6 PUFAs levels were higher in prostate cancer compared with age-matched

control (35). We found total omega-3 PUFAs and omega-6 PUFAs were not associated with prostate cancer risk both African-Americans and Nigerians populations [Table 3]. Our findings were consistent with Männistö et al. (36) report that no overall association between unsaturated fatty acid composition in serum and the risk of prostate cancer.

We found that a total of omega-3 fatty acids were significantly higher among Nigerians, while a total of both *trans* and omega-6 fatty acids were significantly higher among African Americans. Our findings indicate that the higher omega-3 fatty acids among Nigerians may contribute to comparatively lower incidence of prostate cancer in this population. The higher levels of total omega 3 in Nigerians remind us the historical fact that early humans evolved eating fish, probably inter-tidal shellfish, while living a shoreline existence in Africa (37). Still today, fish remains as one of the main sources of protein in Nigeria. There have been several studies of the relationship between prostate cancer and fish consumption, a major source of omega-3 fatty acids. Ecological evidence supporting a negative association comes from population such as Eskimos, who have high intake of fish and low incidence of prostate cancer. According to a study by Parkinson et al., plasma concentrations of total omega-3 fatty acids were 4.3 times higher in Native Alaskans Eskimos than in non-native control subjects. EPA and DPA were 13 and 6.8 times higher, respectively, in Eskimos compared to controls. However, plasma concentrations of omega-6 fatty acids did not differ between Eskimos and controls. (38). Similar assumptions could be postulated for Nigerians where the incidence of prostate cancer remains remarkably lower than African-Americans. Our assumption is substantiated by a prospective study by Chavarro et al. (39) found higher blood levels of

long-chain n-3 fatty acids mainly found in marine foods, and of linoleic acid, main found in non-hydrogenated vegetables oils are associated with a reduced risk prostate cancer.

On the other hand, higher total *trans* and omega-6 fatty acids among African-Americans may be responsible to comparatively higher incidence of prostate cancer in this populations. The plasma level reflects body burden of *trans* fatty acids in terms of intake of hydrogenated oils. For example, Oleic acid is transformed into its *trans* isomer, elaidiac acid, which is most abundant trans fatty acid in most hydrogenated oils. In the USA, refined, processed foodstuffs are flooded with label “partially hydrogenated vegetable oil” contain *trans* form of fatty acids instead of *cis*. In human tissues, *trans* form unsaturated fatty acid behaves as if it were saturated, may has been implicated in prostate cancer risk. Chavarro JE et. al. reported blood levels of total *trans* fatty acids were unrelated to total prostate cancer risk when comparing top to bottom quintile (RR, 2.21 95% CI=1.14-4.29; p=0.06). However, it was revealed that blood levels of *trans* isomers of oleic and linoleic acids are associated with increased risk of non aggressive prostate cancer (40). Therefore, comparative higher values of total *trans* fatty acids may potentially account for higher incidence rate of prostate cancer in African-Americans. Regarding our findings that total omega-6 fatty acids were significantly higher among African-Americans, it is normally expected to be high as of today in the westernized diet the predominant dietary polyunsaturated fatty acids are n-6 fatty acids. In a study it was found link to greater consumption from animal sources to increased risk for prostate cancer among African-Americans (14). This higher status may be partly due to dietary intake because most of individual fatty acids in n-6 family could be endogenously

synthesized in human body except the linoleic acid. Godly et al. found a significant positive association with total omega-6 fatty acids, with adjusted odds ratios and 95 % confidence intervals of 1.0 (reference), 3.6 (1.3-9.7) and 3.5 (1.2-10.2) a case-control study. (41). Laboratories studies shows n-6 fatty acids stimulate prostate tumor growth but the dietary intake of these fatty acids affects prostate cancer risk in human remains unclear (42). But high linoleic acid and low marine fatty oils were not associated with increased with increased risk as previously hypothesized (43).

We found total saturated fatty acids were significantly higher among Nigerians than African-Americans. This findings supported the altered historical patterns of nutrition transition in recent decades leading to the dramatic increase in availability of inexpensive vegetables fats particularly red palm oil resulted from rapid urbanization of west African countries have (44). Still today, *Akara* from Nigeria, a fritter made by frying cowpea flour in palm oil and a rice porridge made with coconut milk are examples of popular dishes in Nigeria (45). These dietary sources of fat in Nigeria may be inclined to sustain higher levels of saturated fatty acids in plasma. In addition, the traditional diet in Nigeria rich in high carbohydrate composition may contribute in stimulated human fatty acid synthesis resulting in higher saturated fatty acid in plasma.

The total omega 9 fatty acids level is recorded higher in Nigerians than African-Americans. This finding may indicate consumption of vegetable oils was comparatively higher among Nigerians than their counterparts. Interestingly, we found in both adjusted

and unadjusted ORs increased across the gradient of quartiles but overall magnitudes remained significantly protective ($P_{\text{trend}} = 0.03$ for adjusted ORs; $P_{\text{trend}} = 0.01$ for unadjusted ORs) among African-Americans. No similar significant trends were observed among Nigerians. Among African-Americans, the most important omega-9 fatty acid, i.e., Oleic acid significantly appeared to be protective in unadjusted ORs (OR 0.38, 95%CI=0.12-1.20; $P_{\text{trend}} = 0.02$). In adjusted ORs it was not significant (OR 0.78, 95%CI=0.19-3.24; $P_{\text{trend}} = 0.05$). No similar trends were observed among Nigerians. Our findings supported the fact that the diets rich in olive oil (a source of oleic acid) might reduce the risk of prostate cancer in certain population (46). On the other hand, erucic acid, an omega-9 fatty acid, appeared to be risk among African-Americans (adjusted OR, 3.96; 95% CI =1.05-14.90; unadjusted OR, 2.95; 95%CI= 1.01-8.60) but not among Nigerians. Presently we do not know any biological explanation for this observation.

We have examined prostate cancer risk according to individual fatty acids. We did not find any risk for myristic acid for both populations contrary to the reports by Männistö et al. (36) and Harvei et al. (47) found high serum myristic acid was associated with a 2-fold risk of prostate cancer. In our study we found no risk associated with palmitic and stearic acids for both populations. Our findings support Physicians' Health Study, plasma palmitic acid and stearic acid had no significant associations with prostate cancer risk (43). A nested case-control study based on stored samples from a serum bank in Norway found a positive association for palmitic acid (OR, 2.3; 95% CI 1.1-4.7, the highest versus lowest quartile) but we did not find such association for both populations (47).

But the results are mixing in direction. Plasma concentration of α -linolenic acid was more than two times higher in among African-Americans than Nigerians. This finding may indicate potential cause of higher incidence rates among African-Americans which are agrees with the finding that a 2.6-fold increased risk for prostate cancer among men in the highest quartile of α -linolenic acid (48). However this hypothesis was not supported by our findings that no risk accounts for α -linolenic in both populations which are contrary of some previous epidemiological studies (43) Harvei et al. investigated pre-diagnostic serum levels of fatty acids among 141 cases and matched controls in Norway. They found an increased risk of prostate cancer with increasing quartiles of a-linolenic acids (ORs=1.0, 1.4., 1.5, 2.0, trend $p=0.03$) but no associations with total omegar-3 or total omega-6 fatty acids (49). Gann et al. performed a nested case-control study of prostate cancer and plasma fatty acids that revealed a significant increasing in risk associated with a-linolenic acid levels (trend $P=0.03$) and other fatty acids, including palmitic stearic, oleic, linoleic, arachidonic and EPA , were unrelated to risk. Our findings were similar to the observation that no overall associations between risk of prostate cancer and total omega-3, EPA, or DHA (48).

We found linoleic acid was not related to the risk for African-Americans (OR=0.77, 95% CI=0.18-3.41) for the highest vs. lowest quintile, $P_{\text{trend}} = 0.24$)but not for Nigerians (OR=0.37, 95%CI=0.15-0.97; $P_{\text{trend}} = 0.07$). These findings contradict that Newcomer et. al found two-fold elevations in risk associated with higher levels of linoleic acid and total omega-6 fatty acids, although neither of these odds ratios achieved statistical significance. We found significant higher plasma concentration of arachidonic acid

among African-Americans may indicate higher consumption of meat by them than their counterparts. Surprisingly, both adjusted and unadjusted ORs for both populations did not signal any risk for them (Table 4 & 5).

The current study has several strengths and weaknesses, which should be considered. The use of population-based controls increases the strengths. There may be some selection bias in collecting pre-treatment clinic or physician's office-based cases, especially in US cases and controls where the status of participation in a study sometimes dictates their more health-consciousness than general men. But similar anticipations were not true in Nigerian counterparts. Although plasma levels of fatty acids are strongly correlated with adipose tissue samples, (49) plasma levels may not accurately reflect levels in target tissues such as prostate. Misclassification of individual's fatty acid level is likely to be random, and therefore, underestimations of any real fatty acid effects are expected to be very unlikely. Both populations have significant anthropometric differences; however, they are not probably confounding our findings. Studies of body build in adults and prostate cancer risk have not shown consistent results (50).

It is not clear whether or not levels of temperature and duration of storage could have affected fatty acid levels in plasma. We stored our samples at -40 °C and -80 °C for two to three years maximum and measured actual concentrations other than red cell membrane profiling. However, Stanford et al (51) have shown that there is no deterioration of fatty acid levels when profiling them in red cell membranes in samples stored at -70 °C for up to 12 months. Even Marangoni F et al. (52) analyzed fatty acids from 14 to 24 carbons

while whole blood samples from fingertips have been preserved at only 4 C until analyzed. The quality of fatty acids under storage even at -25 C has remained surprisingly stable (53).

Many factors have to be taken into account when using serum biomarkers. Individual fatty acids can be measured from erythrocytes, platelets, adipose tissue, and from several lipid subfractions in plasma, such as cholesterol esters, phospholipids, and triglycerides (33). The fatty acid composition varies between fractions. For example, linoleic acid covers half of all fatty acids in the cholesterol ester fraction, and has two to three times higher proportions than that of oleic acid. The linoleic:oleic acid ratio is about two in plasma phospholipids, whereas oleic acid predominates in triglycerides (54). Furthermore, there is more palmitic acid than stearic acid in these substrates, but the ratio between these two fatty acids varies from 2 in plasma phospholipids to >10 in plasma cholesterol esters (55). Thus comparison of results between studies is difficult because fatty acids have often been measured from different fractions. Changes in saturated fatty acids and monounsaturated fatty acids may be depend more on endogenous synthesis than diet. Linoleic and polyunsaturated fatty acids, which are high in the United States diet, may decrease the level of saturated fatty acids as we observed in our result.

CONCLUSIONS

There were significant differences in the plasma concentrations of total fatty acids, total saturated fatty acids, total omega-9, total omega-6, total omega-3, and total *trans* fatty acids between African-Americans and Nigerians. These differences also retained in all other individual fatty acids except for vaccenic and mead acids. We emphasize that the findings of increasing risk for prostate cancer with increasing quartiles of nervonic and behenic acids among Nigerians and total *trans* and erucic acids among African-American should be viewed as tentative and demand further investigations. Larger studies and future laboratory research will clarify the impact, if any of these fatty acids on mechanisms involved in prostate cancer growth and may possibly lead to the development of strategies to reduce risk.

Table 1. Risk of prostate cancer among African-Americans and Nigerians, by selected characteristics.

	African-Americans				Nigerians			
	Cases	Controls	OR	95% CI	Cases	Controls	OR	95% CI
Age (%)								
≤54 years	13.0	63.5	1.00		3.0	46.9	1.00	
55-64 years	41.3	30.2	17.8	4.0-78.7	22.7	27.4	79.4	17-367
65-74 years	30.4	2.1	2.7	0.7-10.4	37.9	18.6	6.20	2.7-14.5
≥75 years	15.2	4.2	0.3	0.04-1.7	36.4	7.1	2.52	1.13-5.63
Family history of PCa (%)	34.9	10.5	4.6	1.8-11.3	4.6	1.8	2.63	0.6-12.0
Education status (%)								
Less than high school	14.0	11.5	1.00		67.7	61.6	1.00	
High school	34.9	42.7	1.36	0.4-4.3	7.7	16.7	1.15	0.5-2.8
Some college	4.7	17.7	2.03	0.9-4.6	12.3	12.0	2.74	0.8-9.5
College/Post-graduate	46.5	28.1	6.3	1.3-30.4	12.3	9.7	1.24	0.4-3.9
Missing data	3				1	10		
Socioeconomic status (%)								
Low	36.4	59.6	1.00		82.5	83.5	1.00	
Moderate	34.1	24.7	3.1	1.2-7.9	11.1	8.5	0.81	0.3-2.5
High	29.5	15.7	1.4	0.5-3.7	6.3	8.0	0.61	0.2-2.5
Missing data	2	7			3	38		

Table 2. Comparison of physiologically abundant plasma fatty acids concentrations (µg/ml)[†] between African-Americans and Nigerians.

	Africans-Americans		Nigerians	
Total fatty acids*	2,597.94	(2,306.2, 3034.8)	2,419.95	(2,063.8, 2,795.1)
Total saturated fatty acids*	774.73	(695.3, 933.8)	860.43	(738.9, 989.9)
Total n-9 fatty acids*	519.30	(446.2, 617.8)	615.52	(524.6, 763.2)
Total n-6 fatty acids*	1,085.45	(939.9, 1,243.3)	665.31	(552.7, 788.4)
Total n-5 & n-7 fatty acids	94.32	(75.4, 124.5)	98.23	(77.8, 135.5)
Total n-3 fatty acids*	85.28	(68.3, 116.1)	99.72	(74.0, 144.8)
Total <i>trans</i> fatty acids*	61.48	(42.9, 90.6)	15.34	(11.9, 20.1)
Lauric acid*	1.23	(0.9, 1.9)	4.24	(2.6, 8.2)
Myristic acid*	16.16	(12.2, 24.4)	23.58	(16.3, 37.0)
Palmitic acid*	504.77	(453.4, 607.9)	585.60	(515.7, 670.5)
Stearic acid*	191.95	(170.2, 231.6)	179.43	(152.2, 211.5)
Palmitoleic acid*	35.18	(27.1, 59.2)	57.18	(40.5, 84.8)
Oleic acid*	471.03	(401.7, 566.9)	560.84	(473.2, 696.4)
Vaccenic acid	39.50	(32.7, 48.4)	39.52	(31.2, 50.1)
Nervonic acid*	25.94	(21.4, 30.4)	31.22	(26.1, 37.9)
Linoleic acid*	763.07	(655.2, 882.4)	496.22	(415.5, 584.3)
γ- linolenic acid*	12.49	(9.36, 16.8)	7.00	(4.46, 10.44)
Di-homo-γ- linolenic acid *	38.86	(33.0, 48.4)	27.07	(20.8, 35.6)
Mead acid	3.35	(2.5, 4.7)	3.53	(1.9, 5.6)
Arachidonic acid*	241.67	(202.5, 289.3)	113.55	(83.0, 146.0)
α-linolenic acid*	14.76	(11.2, 19.7)	5.03	(3.8, 7.0)
Eicosapentaenoic acid*	12.68	(7.8, 19.1)	21.56	(13.2, 37.4)
Docosapentaenoic acid*	7.04	(5.4, 9.1)	2.94	(1.9, 4.1)
Docosaheptaenoic acid*	44.75	(31.1, 62.7)	58.78	(43.1, 80.1)

[†]Values expressed as median [25th-75th percentile]

* *P*-values <0.001

Table 3. Odds ratios[§] and 95% confidence intervals (CIs) for prostate cancer risk in quartiles of plasma fatty acid concentrations (µg/ml) between African-Americans and Nigerians.

	African-Americans			Nigerians		
	OR	95% CI	$P_{\text{trend}}^{\dagger}$	OR	95% CI	$P_{\text{trend}}^{\dagger}$
Total fatty acids						
Quartile 1 (lowest)	1.00			1.00		
Quartile 2	0.37	(0.13-1.03)		1.54	(0.72-3.31)	
Quartile 3	0.42	(0.15-1.20)		1.68	(0.77-3.64)	
Quartile 4 (highest)	1.07	(0.35-3.26)	0.08	1.20	(0.57-2.54)	0.54
Total saturated fatty acids						
Quartile 1 (lowest)	1.00			1.00		
Quartile 2	0.50	(0.18-1.34)		1.89	(0.83-4.29)	
Quartile 3	1.04	(0.37-2.95)		1.21	(0.56-2.59)	
Quartile 4 (highest)	1.17	(0.42-3.28)	0.28	1.06	(0.50-2.24)	0.44
Total n-9 fatty acids						
Quartile 1 (lowest)	1.00			1.00		
Quartile 2	0.16	(0.05-0.50)		1.46	(0.68-3.16)	
Quartile 3	0.29	(0.09-0.95)		1.37	(0.64-2.94)	
Quartile 4 (highest) *	0.42	(0.13-1.38)	0.01	1.23	(0.57-2.65)	0.78
Total n-7 & n-5 fatty acids						
Quartile 1 (lowest)	1.00			1.00		
Quartile 2	0.19	(0.06-0.55)		1.07	(0.46-2.52)	
Quartile 3	0.60	(0.20-1.82)		0.49	(0.23-1.07)	
Quartile 4 (highest) *	0.61	(0.21-1.81)	0.01	0.92	(0.41-2.07)	0.14
Total n-6 fatty acids						
Quartile 1 (lowest)	1.00			1.00		
Quartile 2	0.53	(0.20-1.40)		1.41	(0.65-1.72)	
Quartile 3	0.64	(0.23-1.78)		2.33	(1.00-5.41)	
Quartile 4 (highest)	1.35	(0.46-3.93)	0.26	0.92	(0.45-1.89)	0.13
Total n-3 fatty acids						
Quartile 1 (lowest)	1.00			1.00		
Quartile 2	3.31	(1.17-9.40)		0.67	(0.31-1.42)	
Quartile 3	2.38	(0.87-6.50)		0.90	(0.41-1.97)	
Quartile 4 (highest)	1.49	(0.56-3.96)	0.11	1.11	(0.50-2.46)	0.60
Total <i>trans</i> fatty acids						
Quartile 1 (lowest)	1.00			1.00		
Quartile 2	0.11	(0.03-0.44)		0.79	(0.35-1.79)	
Quartile 3	0.30	(0.07-1.29)		1.55	(0.63-3.83)	
Quartile 4 (highest) **	0.92	(0.17-5.02)	0.00	1.49	(0.62-3.61)	0.35

[§]Unadjusted values.

[†]Calculated with median fatty acid concentration in each quartile as a continuous variable.

* P -value <0.05

** P -value <0.001

Table 4. Odds ratios[§] and 95% confidence intervals (CIs) for prostate cancer risk in quartiles of plasma fatty acid concentrations (µg/ml) between African-Americans and Nigerians.

	African-Americans			Nigerians		
	OR	95% CI	<i>P</i> _{trend} [†]	OR	95% CI	<i>P</i> _{trend} [†]
Total fatty acids						
Quartile 1 (lowest)	1.00			1.00		
Quartile 2	0.60	(0.15-2.33)		0.79	(0.30-2.02)	
Quartile 3	0.52	(0.15-1.85)		1.32	(0.51-3.41)	
Quartile 4 (highest)	2.17	(0.52-9.05)	0.29	0.80	(0.33-1.98)	0.69
Total saturated fatty acids						
Quartile 1 (lowest)	1.00			1.00		
Quartile 2	0.53	(0.14-2.00)		1.16	(0.43-3.10)	
Quartile 3	1.72	(0.42-7.01)		1.17	(0.47-2.92)	
Quartile 4 (highest)	1.82	(0.49-6.70)	0.25	1.05	(0.42-2.57)	0.98
Total n-9 fatty acids						
Quartile 1 (lowest)	1.00			1.00		
Quartile 2	0.16	(0.04-0.66)		0.77	(0.29-2.05)	
Quartile 3	0.43	(0.10-1.77)		0.84	(0.33-2.11)	
Quartile 4 (highest)*	0.92	(0.21-3.95)	0.03	0.80	(0.32-2.05)	0.95
Total n-7 & n-5 fatty acids						
Quartile 1 (lowest)	1.00			1.00		
Quartile 2	0.30	(0.08-1.23)		0.87	(0.31-2.47)	
Quartile 3	0.85	(0.22-3.25)		0.33	(0.13-0.86)	
Quartile 4 (highest)	0.55	(0.15-2.05)	0.34	0.82	(0.31-2.21)	0.07
Total n-6 fatty acids						
Quartile 1 (lowest)	1.00			1.00		
Quartile 2	0.80	(0.23-2.76)		0.64	(0.24-1.72)	
Quartile 3	0.68	(0.20-2.35)		2.36	(0.78-7.12)	
Quartile 4 (highest)	1.46	(0.17-1.26)	0.73	0.54	(0.22-1.34)	0.05
Total n-3 fatty acids						
Quartile 1 (lowest)	1.00			1.00		
Quartile 2	1.33	(0.36-4.91)		0.50	(0.20-1.27)	
Quartile 3	2.12	(0.52-8.74)		0.70	(0.27-1.82)	
Quartile 4 (highest)	0.74	(0.21-2.60)	0.48	0.92	(0.36-2.35)	0.47
Total <i>trans</i> fatty acids						
Quartile 1 (lowest)	1.00			1.00		
Quartile 2	0.09	(0.01-0.69)		0.42	(0.15-1.19)	
Quartile 3	0.49	(0.06-4.05)		1.08	(0.34-3.41)	
Quartile 4 (highest)*	4.09	(0.28-59.59)	0.02	1.52	(0.50-4.65)	0.11

[§]Adjusted for age, levels of education, family history of prostate cancer, and waist-hip ratios.

[†]Calculated with median fatty acid concentration in each quintile as a continuous variable.

**P*-value <0.05

Table 5. OR[§] of prostate cancer comparing lowest to highest quartiles of plasma fatty acid concentrations (µg/ml) between African-Americans and Nigerians.

	African-Americans			Nigerians		
	OR	95% CI	<i>P</i> _{trend} [†]	OR	95% CI	<i>P</i> _{trend} [†]
C12:0 Lauric acid	0.86	(0.32-2.33)	0.13	1.21	(0.56-2.59)	0.66
C14:0 Myristic acid ^{**}	0.86	(0.32-2.31)	0.00	1.47	(0.64-3.34)	0.54
C16:0 Palmitic acid	0.59	(0.20-1.75)	0.09	1.50	(0.71-3.19)	0.31
C18:0 Stearic acid	0.77	(0.28-2.11)	0.93	1.48	(0.70-3.12)	0.26
C22:0 Behenic acid ^{**}	1.14	(0.40-2.24)	0.80	2.94	(1.35-6.41)	0.00
C16:1 Palmitoleic acid [*]	0.16	(0.05-0.55)	0.02	1.13	(0.49-2.61)	0.13
C18:1 Oleic acid [*]	0.38	(0.12-1.20)	0.02	1.49	(0.68-3.28)	0.74
C18:1 <i>cis</i> -Vaccenic acid ^{**}	1.12	(0.39-3.24)	0.00	1.04	(0.49-2.20)	0.30
C24:1 <i>cis</i> -Nervonic acid ^{**}	2.56	(0.94-7.00)	0.02	2.41	(1.20-4.84)	0.00
C18:1 n-9; <i>cis</i> -Erucic acid ^{**}	2.95	(1.01-8.60)	0.07	1.06	(0.52-2.14)	0.00
C20:3 n-9; <i>cis</i> -Mead acid [*]	0.42	(0.13-1.34)	0.01	0.72	(0.33-1.59)	0.87
C16:1 n-9; <i>trans</i> -Palmitelaidic acid [*]	0.63	(0.22-1.74)	0.02	1.00	(0.44-2.27)	0.44
C18:1 n-9; <i>trans</i> -Elaidic acid [*]	0.13	(0.01-1.12)	0.02	1.03	(0.44-2.41)	0.52
C18:2 n-6 Linoleic acid [*]	0.36	(0.11-1.16)	0.03	0.84	(0.40-1.75)	0.56
C18:3 n-6 γ-linolenic acid	0.54	(0.19-1.59)	0.05	2.03	(0.91-4.54)	0.15
C20:3 n-6 Dihomo-γ-linolenic acid	0.46	(0.15-1.40)	0.10	1.30	(0.62-2.72)	0.12
C20:4 n-6 Arachidonic acid ^{**}	0.46	(0.17-1.23)	0.11	0.74	(0.37-1.50)	0.00
C18:3 n-3 α-linolenic acid	1.00	(0.37-2.73)	0.95	1.21	(0.57-2.59)	0.85
C20:5 n-3 Eicosapentaenoic acid	1.26	(0.45-3.46)	0.64	0.81	(0.35-1.88)	0.05
C22:5 n-3 Docosapentaenoic acid	0.88	(0.32-2.40)	0.54	1.16	(0.56-2.39)	0.12
C22:6 n-3 Docosahexaenoic acid ^{**}	1.57	(0.60-4.12)	0.00	0.75	(0.35-1.62)	0.87

[§]Unadjusted values

[†]Calculated with median fatty acid concentration in each quintile as a continuous variable.

^{*}*P*-value <0.05

^{**}*P*-value <0.00

Table 6. OR[§] of prostate cancer comparing lowest to highest quartiles of plasma fatty acid concentrations (µg/ml) between African-Americans and Nigerians.

	African-Americans			Nigerians		
	OR	95% CI	<i>P</i> _{trend} [†]	OR	95% CI	<i>P</i> _{trend} [†]
C12:0 Lauric acid	2.95	(0.75-11.66)	0.12	1.34	(0.53-3.35)	0.57
C14:0 Myristic acid [*]	0.70	(0.20-2.42)	0.03	1.97	(0.73-5.29)	0.55
C16:0 Palmitic acid	1.05	(0.27-4.06)	0.35	1.38	(0.55-3.45)	0.89
C18:0 Stearic acid	1.11	(0.32-3.84)	1.00	1.42	(0.58-3.48)	0.12
C22:0 Behenic acid [*]	1.14	(0.30-4.30)	0.55	2.42	(0.95-6.15)	0.01
C16:1 Palmitoleic acid	0.20	(0.05-0.86)	0.14	1.07	(0.39-2.96)	0.16
C18:1 Oleic acid	0.78	(0.19-3.24)	0.05	1.49	(0.57-3.91)	0.75
C18:1 <i>cis</i> -Vaccenic acid [*]	1.12	(0.31-4.03)	0.03	0.48	(0.19-1.23)	0.33
C24:1 <i>cis</i> -Nervonic acid ^{**}	2.13	(0.59-7.69)	0.09	1.83	(0.82-4.10)	0.00
C18:1 n-9; <i>cis</i> -Erucic acid	3.96	(1.05-14.90)	0.05	0.91	(0.39-2.12)	0.14
C20:3 n-9; <i>cis</i> -Mead acid	0.54	(0.13-2.15)	0.31	0.36	(0.14-0.96)	0.24
C16:1 n-9; <i>trans</i> -Palmitelaidic acid	0.68	(0.19-2.48)	0.31	1.52	(0.57-4.06)	0.28
C18:1 n-9; <i>trans</i> -Elaidic acid	0.66	(0.05-8.73)	0.09	1.00	(0.34-2.93)	0.19
C18:2 n-6 Linoleic acid	0.77	(0.18-3.41)	0.24	0.37	(0.15-0.97)	0.07
C18:3 n-6 γ-linolenic acid	0.60	(0.16-2.26)	0.09	1.74	(0.64-4.71)	0.48
C20:3 n-6 Dihomo-γ-linolenic acid	0.62	(0.16-2.34)	0.65	0.86	(0.35-2.08)	0.21
C20:4 n-6 Arachidonic acid [*]	0.30	(0.08-1.11)	0.02	0.72	(0.31-1.67)	0.05
C18:3 n-3 α-linolenic acid	1.30	(0.37-4.58)	0.95	1.03	(0.42-2.52)	0.89
C20:5 n-3 Eicosapentaenoic acid	0.82	(0.21-3.24)	0.33	1.04	(0.38-2.82)	0.06
C22:5 n-3 Docosapentaenoic acid	1.01	(0.31-3.33)	0.78	1.04	(0.44-2.46)	0.59
C22:6 n-3 Docosahexaenoic acid	1.35	(0.40-4.61)	0.28	0.56	(0.22-1.40)	0.34

[§]Adjusted for age, levels of education, family history of prostate cancer, and waist-hip ratios.

[†]Calculated with median fatty acid concentration in each quintile as a continuous variable.

^{*}*P*-value <0.05

^{**}*P*-value <0.001

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Original Article

Prevalence of elevated serum prostate specific antigen in rural Nigeria

FLORA UKOLI,¹ USIFO OSIME,³ FOLASADE AKEREYENI,³ OSAZUWA OKUNZUWA,⁴ RICK KITTLES² AND LUCILE ADAMS-CAMPBELL¹

¹Cancer Center and ²National Human Genome Center, Howard University, Washington DC, USA, ³Department of Surgery, University of Benin Teaching Hospital, Benin-City and ⁴Osse Health Clinic, Osse, Nigeria

Abstract

Background: Recent hospital and cancer registry data show increasing prostate cancer incidence in Nigeria, which was previously regarded as a low incidence region. This study investigates the prevalence of prostate cancer risk in a previously unscreened cohort of rural Nigerians.

Methods: Rural Nigerian men, 40 years and older, were screened by serum prostate specific antigen (PSA) and digital rectal examination (DRE) and those with PSA ≥ 4 ng/mL and/or abnormal DRE were referred for prostate biopsy.

Results: Of 200 consecutive men invited 151 (75.5%) presented for screening, the mean age was 56.45 ± 15.1 and 95 (61.6%) were ≥ 50 years of age. Of the 140 who consented to a blood test, PSA correlated with age ($r = 0.3$, $P < 0.01$), 14 (10.0%) had abnormal PSA ≥ 4 ng/mL, increasing from 3 (3.6%) in men < 60 years to 4 (50%) in men ≥ 80 years. The rate was 13 (15.7%) for men ≥ 50 years and there was no evidence of increased incidence of prostatitis in the community. Mean (median) PSA in ng/mL increased from 1.17 (0.60) in the youngest to 13.75 (4.45) in the oldest cohort. Of those who accepted DRE, 38 (29.0%) had enlarged prostate, including two nodular prostate, one-third with symptoms, increasing from 4 (5.4%) in those < 50 years to 6 (75.0%) in men ≥ 80 years. The proportion of men with PSA ≥ 4 ng/mL among those with enlarged vs. normal prostate is 27.0 to 3.4%, $P < 0.001$, and the pattern was similar for men ≥ 60 years and those < 60 years of age. The 40 (32.0%) men referred for prostate biopsy defaulted mainly because they did not fully understand the need for further investigation because they were symptom free or afraid of the possible side-effects of the procedure or diagnosis of cancer.

Conclusion: The proportion of men with PSA ≥ 4 ng/mL is comparable to that of previously unscreened populations with high incidence of prostate cancer such as African-American men. A larger study is required to confirm these findings and intensify efforts to determine the prostate cancer detection rate by biopsy in this population. A prostate cancer awareness and education campaign will be useful in this community.

Key words Africa, black, digital rectal examination, prostate cancer, prostate specific antigen, Nigeria.

Introduction

Prostate cancer rates in African-American^{1,2} and Afro-Caribbean black men³ have been reported to be high, suggesting genetic predisposition. However, only 10%

of prostate cancer is due to the familial or genetic type, while 90% is considered sporadic, due to the combination or interaction of environmental and genetic factors. Rates of latent prostate cancer are similar all over the world, while the prevalence of the aggressive form varies, emphasizing the importance of cancer-promoting rather than cancer-initiating environmental factors.⁴

Most reports from West African countries like Nigeria are descriptive hospital data reporting increasing incidence of prostate cancer.^{5–8} The recently reported

Correspondence: Flora Ukoli MBBS DPH MPH, Howard University Cancer Center, 2041 Georgia Avenue, NW, Washington DC 20060, USA. Email: fukoli@Howard.edu

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population incidence rate derived from cancer register data is 127/100 000 with a mean age 68.3 ± 9.4 years and a median age of 67.5 years.^{5,9} From autopsy studies, the age-adjusted incidence rate of invasive carcinoma was higher among African Americans than in Africans.¹⁰ Some reasons for this finding may be incomplete detection of cases that never presented in hospitals or patients lost to follow-up on discharge who later died at home, lower life expectancy and selection bias for routine autopsies.

Developing countries like Nigeria now appear to be undergoing a cancer epidemic similar to that in developed countries. Reasons for the low incidence in the past could be due to under reporting and lack of adequate diagnosis. Although the impact of lifestyle changes have not been studied, increased smoking and alcohol use, dietary change to a mixture of traditional Nigerian and Western foods, consumption of foods with additives and increased use of processed beverages are proposed as possible risk factors.¹¹ Prostate cancer that was second only to liver cancer is presently the most common cancer among men over 18 years of age, with an increased relative frequency ratio of 13.2% in 1980–1988 to 16.14% in 1989–1996.⁹ For valid international comparisons, a uniform standard of data collection is required as well as complete national health and census statistics. In the absence of such data, this cross-sectional study investigates the pattern of prostate specific antigen (PSA) distribution in a defined rural West-African community in southern Nigeria in men 40 years and older. There are over 45 distinct ethnic groups in Nigeria, and although people migrate all over the country, there is a tendency for ethnic homogeneity in rural communities.

Methods

Selection of study population

This study was carried out in Edo state, southern Nigeria, in a rural community where 84.7% of the men interviewed were of the Edo tribe. The other men were Urhobos, Itsekiris and Yorubas from the neighboring Delta state. All of the men reported that their grandparents were Nigerians.

The first 200 men who were 40 years and older from consecutive houses and households in a rural Nigerian community, starting from the house of the village head, were informed about a health survey that would require a blood test and digital rectal examination by a public health nurse who resided in that village. Interested men who signed the consent form after reading or having it

read to them were scheduled for a clinic visit. A conscious attempt was made at initial contact to use 'medical check-up', 'disease of the prostate' or 'conditions that affect urination in elderly men' rather than 'prostate cancer screening'. Those who did not consent immediately were given a copy of the consent form to read in their own time and discuss with their family and friends, and were asked to come to the local health center if they decided to participate. The study was approved by the institutional review board (IRB) of Howard University, Washington DC, and by the Research Ethics Committee of the University of Benin Teaching Hospital, Nigeria.

Measures

The questionnaire, which consisted of questions regarding demographic details, medical, dietary and family history of prostate and other cancers, history of tobacco and alcohol use and physical measurements, was completed by trained interviewers. For men who did not have official birth records, the interviewers cross-checked the self-declared age by adding age at first marriage, years before birth of first living child and age of first child in addition to using other historical milestones to check year of birth. A physician observing all precautions against transmission of blood borne pathogens collected 30 mL of venous blood with a multiple draw vacutainer needle into three specimen tubes. The participants then underwent a digital rectal examination (DRE) conducted by the study surgeon who has many years of urology experience, and consulted him regarding urination problems. The DRE was carried out using a lubricated gloved index finger while the patient lay on their side with both legs flexed. The prostate size, presence of a sulcus, consistency and nodularity was recorded on a form.

The blood samples were centrifuged for 15 min after standing for a minimum of 30 min. Serum was then pipetted into 2 mL microvials, packed in cardboard storage boxes and transported on ice within 3 h of collection to be stored in a freezer for up to 3 months until transported on dry ice to Howard University laboratory where they were stored at -70°C . The microvials of serum were then sent to a registered commercial laboratory for PSA analysis by the microparticles enzyme immunoassay technology.¹²

Individual result sheets, including follow-up recommendation, were hand-delivered to each participant by the community health nurse with a detailed explanation of their results. Those with abnormal results were encouraged to consult the doctor at their local health center for counselling. The doctor counselled them with regard to further investigations and the need for and

safety of prostate biopsy before referral to the surgeon and urologist at the teaching hospital. Participants were informed that they would only pay the usual hospital fee and not be charged for the biopsy procedure, histology report or antibiotics.

Statistical analysis

The demographic, medical and other personal information were analyzed and summarized as frequency counts and percent. Mean and median PSA were calculated and compared across various subgroups using the two-sample independent *t*-test and Mann–Whitney *U*-test, respectively. PSA was summarized as grouped data classified into four levels: < 2.5, 2.5–3.9, 4.0–9.9 and ≥ 10 ng/mL. For statistical analysis by χ^2 test, participants were dichotomized into two groups for PSA (< 4 ng/mL and ≥ 4 ng/mL), two groups for DRE (normal and enlarged/abnormal) and two groups for age (< 60 years and ≥ 60 years). All calculations were conducted using SPSS 8.0, Windows version (SPSS, Chigaco, IL, USA).

Results

Of the 176 (88%) men who consented, 151 (85.7%) presented for the study. Five (3.3%) men did not state their age, while PSA for 11 (7.3%) and DRE for 20 (13.2%) were not available due to the patient's refusal or rescheduling difficulty. Those who did not complete the survey were not demographically different from those who did. Eighty-five (56.3%) had lived in their rural town for 20 years or longer, 108 (71.6%) were full-time or part-time farmers, 44 (29.2%) were skilled and semiskilled artisans, 16 (10.6%) were teachers and administrative assistants, 7 (4.6%) were senior administrators/businessmen and 10 (6.6%) were retired. Their ages ranged from 40 to 110 years, with a mean age of 56.45 ± 15.1 years, while 95 (61.6%) of the men were ≥ 50 years.

Of the cigarette smokers, 45 (69.3%) smoked < 5 cigarettes per day, 13 (20%) smoked between 5 and 10 and 7 (10.8%) smoked a pack or more per day. Of the 57 (37.7%) who drank alcohol regularly, 33 (21.9%) drank more than 5 drinks at an occasion once in the last month; a drink of alcohol being 12 ozs (approximately 355 mL) of beer, a glass of wine or a shot of liquor. Half of the men had fewer than seven children while others had between seven and 40 children as a result of polygamy and remarriage. Mean (median) PSA ng/mL increased from 1.17 (0.60) in the youngest to 13.75 (4.45) in the oldest age cohort (Table 1).

Of the 140 who consented to a blood test, PSA ranged from 0.1 to 64.8 ng/mL, 14 (10.0%) had abnormal PSA ≥ 4 ng/mL, increasing from 3 (3.6%) in men < 60 years to 4 (50%) among men ≥ 80 years (Table 2). PSA correlated with age among those with normal PSA ($r = 0.3$, $P < 0.01$) and abnormal PSA ($r = 0.4$, $P < 0.1$). Men ≥ 60 years had a higher proportion of abnormal PSA ≥ 4 ng/mL compared to men < 60 years 20.8% compared to 3.6% ($\chi^2 10.3$, $P < 0.001$).

The rates for enlarged prostate, with or without symptoms, increased from 4 (5.4%) in the youngest to 6 (75%) in the oldest age group (Table 3). Men ≥ 60 years had a higher proportion of enlarged/abnormal prostate on DRE compared to men < 60 years, 49% compared to 16.5% ($\chi^2 15.9$, $P < 0.001$). More men with enlarged prostate gave a history of urinary problems compared to those with normal size prostate, 11 (28.9%) compared to 7 (7.5%), $P < 0.004$. The respec-

Table 1 Mean and median prostate-specific antigen (PSA) by demographic characteristics the study population in rural Nigeria

	<i>n</i> (%) <i>n</i> = 151	PSA ng/mL Mean (median)
Age		
< 50	56 (37.1)	1.17 (0.60)
50–59	34 (22.5)	1.57 (0.55)
60–69	32 (21.2)	2.05 (0.90)
70–79	16 (10.6)	5.69 (1.25)
≥ 80	8 (5.3)	13.75 (4.45)
Not recorded	5 (3.3)	0.55 (0.60)
Educational status		
0–6 years	61 (40.4)	4.60 (1.10)
6–9 years	60 (39.7)	1.74 (0.60)
High school	16 (10.6)	0.75 (0.55)
Technical training	10 (6.6)	0.62 (0.60)
College/graduate	4 (2.7)	1.43 (1.80)
Marital status		
Single	2 (1.3)	*
Married (1 wife)	94 (62.3)	1.92 (0.70)
Married (> 1 wife)	47 (31.1)	3.97 (0.75)
Separated/divorced	6 (4.0)	0.96 (0.60)
Widowed	2 (1.3)	*
Alcohol use		
Regular	56 (37.1)	2.38 (0.70)
Occasional	68 (45.0)	1.92 (0.70)
None	24 (15.9)	5.90 (0.60)
Tobacco use		
Cigarettes	65 (43.0)	1.57 (0.70)
Sniff	26 (17.2)	2.48 (0.70)
Chew	1	*
Cigar	1	*
None	52 (34.4)	4.35 (1.00)

*Mean (median) not calculated for $n < 4$.

Table 2 Prostate-specific antigen (PSA) distribution of rural Nigerian men by age group

PSA (ng/mL)	Age group <i>n</i> (%)				Total <i>n</i> (%)
	< 60	60–69	70–79	≥ 80	
0.0–2.4	75 (90.4)	20 (69.0)	9 (56.2)	2 (25.0)	106 (77.9)
2.5–3.9	5 (6.0)	6 (20.7)	3 (18.8)	2 (25.0)	16 (11.8)
4.0–9.9	0 (0.0)	2 (6.9)	1 (6.2)	2 (25.0)	5 (3.7)
≥ 10	3 (3.6)	1 (3.4)	3 (18.8)	2 (25.0)	9 (6.6)
Total	83	29	16	8	136
%	61.0	21.3	11.8	5.9	100.0

Table 3 Distribution pattern of prostate status by digital rectal examination (DRE) of rural Nigerian men by age group

DRE	Age group <i>n</i> (%)				Total <i>n</i> (%)
	< 60	60–69	70–79	≥ 80	
Norma	66 (83.5)	19 (65.5)	5 (35.7)	2 (25.0)	192 (70.2)
Enlarged					
No symptoms	10 (12.7)	7 (24.1)	6 (42.9)	1 (12.5)	24 (18.3)
With symptoms	3 (3.8)	3 (10.3)	3 (21.4)	3 (37.5)	12 (9.2)
Nodular (susp of cancer)	0	0	0	2 (25.0)	2 (1.5)
Total	79	29	14	8	131
%	60.3	22.1	10.7	6.1	100.0

susp, suspicious.

Table 4 Prostate-specific antigen (PSA) distribution by prostate status by digital rectal examination (DRE) of rural Nigerian men

PSA (ng./mL)	Prostate status (DRE) <i>n</i> (%)				Total <i>n</i> (%)
	Normal	Enlarged no symptom	Enlarged with symptoms	Nodular (susp, of cancer)	
0.0–2.4	79 (84.9)	14 (58.3)	3 (25.0)	1 (50.0)	97 (77.6)
2.5–3.9	6 (6.5)	7 (29.2)	2 (16.7)	0	15 (12.0)
4.0–9.9	1 (1.1)	1 (4.2)	2 (16.7)	0	4 (3.2)
≥ 10.0	2 (2.2)	2 (8.3)	4 (33.3)	1 (50.0)	9 (7.2)
Total	88	24	11	2	125
%	70.4	19.2	8.8	1.6	100.0

susp, suspicious.

tive rate for history of symptoms was 12 (22.2%) compared to 6 (6.8%), $P < 0.01$, in men ≥ 60 compared to men < 60 years. The proportion of men with PSA ≥ 4 ng/mL was not statistically different for men with or without history of urinary symptoms in both the younger and the older group, 1 (16.7%) compared to 2 (2.7%) and 8 (20.5%) compared to 3 (25%), respectively. The major urinary symptoms were frequency 5 (27.8%), straining, difficulty or pain starting urination 5 (27.8%), weak urinary stream 3 (16.7%), urethritis 3 (16.7%) and dribbling 2 (11.1%). There was no report of symptoms suggestive of acute or chronic prostatitis.

Three (3.4%) men with normal prostate on DRE, 9 (25.7%) with enlarged prostate, one with hard indurated prostate and one who refused DRE had abnormal PSA (≥ 4 ng/mL, $P < 0.001$) (Table 4). This pattern was similar for men < 60 years (χ^2 6.0, $P < 0.015$) and those ≥ 60 years (χ^2 4.2, $P < 0.04$). At least 40 (32%) had abnormal PSA and/or DRE warranting referral for prostate biopsy. The mean (median) PSA ng/mL for men with enlarged prostate was statistically higher than for men with normal prostate in both the younger and older cohorts, 3.13 (1.40) to 1.05 (0.06), $P < 0.01$ and 7.92 (2.60) to 2.19 (0.65), $P < 0.01$, respectively.

Discussion

This study is one of the first to conduct prostate cancer 'case-finding' in a previously unscreened rural community in Nigeria using serum PSA as the biomarker in combination with DRE examination performed by an experienced surgeon. Apart from the small sample size, a major limitation of this study was the lack of prostate biopsy follow-up information. That 40 (32%) men had abnormal PSA and/or DRE is an important finding, especially when 9 (6.6%) of the men had a PSA over 10 ng/mL. The men with abnormal PSA are yet to present for prostate biopsy, primarily because they do not understand the need for the investigation, especially when they are symptom free. There has been no public awareness campaign about prostate cancer in the country and having been told that the prostate is one of the male reproductive glands, irrational fear of impotence resulting from any surgery or procedure in the anorectal region cannot be ruled out.

The situation however, is different for a condition like breast cancer where the awareness level has been raised by recent campaigns in Nigeria, the breast being more accessible for examination and biopsy, and availability of fine needle aspiration technique, which is less invasive.¹³ Until public awareness of the necessity and safety of prostate biopsy is raised enough for symptom free men to accept the procedure for diagnostic purposes, the rate of abnormal PSA will have to serve as a crude index of the prevalence of prostate cancer risk. A major assumption in this study is that the cut-off point of 4 ng/mL is appropriate for the population. PSA is known to increase with age and size of prostate, and values over 10 ng/mL are suspicious of cancer, regardless of age and prostate size. Even if ultrasound facility was readily available to this rural community, PSA density has not been shown to have superior predictive value for prostate cancer over total PSA.

International comparison of percentage population at higher risk for prostate cancer from published literature is complicated by the differences in the age range included in PSA-based screenings and PSA cut-off point above which the participant is classified as abnormal. The usual cut-off point in most studies is PSA ≥ 4 ng/mL or PSA > 4 ng/mL, while fewer studies use PSA ≥ 10 ng/mL or PSA ≥ 2 ng/mL. Studies can recruit a few hundred or less, as in single practice screenings, or include thousands of men as in multicenter studies; from a one-day screening to screenings that span several years. Regular or serial PSA-based prostate cancer screening over time will lead to a decrease in the proportion of men with abnormal test results. The prostate cancer detection rate will also decrease to near the

population-based incidence rate.¹⁴ The proportion of men with abnormal PSA in this population-based screening will, therefore, be a prevalence rate as there had been no routine screening in the past.

In the last two decades, population-based PSA-based screenings in the US that included men 50 years and older reported abnormal PSA rates > 4 ng/mL of 10–15%.^{15–18} Reports from the Netherlands¹⁹ and Singapore²⁰ were similar but included people with PSA ≥ 4 ng/mL and rates from Germany²¹ and Sweden²² are 17–17.2%, prostate cancer detection rates ranged from 2.1 to 4.6%. In a South African study that included 4.5% black Africans, an abnormal PSA rate of 15.2% and a prostate cancer detection rate of 3.5% overall and 8.5% for black men was reported.²³ The prevalence of abnormal PSA ≥ 4 ng/mL in these Nigerian men, ≥ 50 years of age, is comparable at 15.7%. Including men 40 years upwards, the rate is 10%, comparable to the 8% rate for slightly younger African Americans, mean age 55 years, in Detroit.²⁴ These rates are quite different from the lower rate of 3.4% with prostate cancer detection rate of 1.3% in Japan, using an ethnic specific PSA cut-off point of ≥ 2 ng/mL to detect half of the cases.²⁵

Other authors from Nigeria who conducted a hospital based study reported a very low rate of 1 (1.7%) for abnormal PSA ≥ 4 ng/mL among the controls who were aged 22–76 years and that no man younger than 50 years had a PSA > 2 ng/mL.²⁶ In our study, 5 (9.4%) men below 50 years had a PSA > 2 ng/mL. This divergent finding is not surprising as controls recruited in a hospital setting are not representative of the general population and the inclusion of very young men under 40 years. However, the rate of abnormal PSA among men with clinical BPH in that study was 63% compared to 50% for men with enlarged prostate with symptoms in this study but 26% for all men with enlarged prostate. This disparity is also expected because our study included men with mild to moderate prostate enlargement, two-thirds without symptoms. The men in the referenced study had symptoms that warranted hospital visit suggestive or more severe prostate pathology.²⁶

The prostate cancer incidence rate of 127/100 000 for Nigeria,^{5,9} histological evidence of prostate cancer in 14.8% of Nigerian patients with prostatism,²⁷ that prostate cancer has become the number one cancer in Nigerian men,²⁸ and an estimated age-adjusted prostate cancer incidence rate of 93.8/100 000 in Cameroon,²⁹ could be conservative rates as they have been derived from hospital data and prostate cancer is a 'silent' disease that may not come to medical attention. However, in Algeria prostate cancer is the fifteenth cancer among Arab men, and in Zimbabwe, it is the fifth cancer in Africans but the second cancer for Europeans.³⁰

Although cancer incidence data from Africa is sparse, available information indicates much geographic variation. The few population-based cancer registers in Africa that report incidence rates to the International Association of Cancer Registry (IARC) are not reliable because of inconsistency in data collection leading to poor data quality.^{13,30,31} In comparison with other regions of the world, prostate cancer incidence per 100 000 in Africa, Senegal is 4.3 compared to 4.9 for Japan, 22.2 for Brazil and 100.2 for African Americans.³¹ The Dakar Cancer Registry in Senegal was established in 1968.

The first cancer registry in Nigeria was founded in Ibadan in 1960, the Nigerian Cancer Society in 1968 and these bodies initiated the collection of cancer statistics among other objectives. In 1960, the crude cancer incidence rate for Ibadan, Nigeria, was 33.7 per 100 000 for males and 45.1 for females.¹¹ Between 1960 and 1980, prostate cancer was diagnosed third to non-Hodgkin's lymphoma and liver cancer. Cancer registration was incomplete because of lack of case notification. Registry staff actively collected data from different health institutions but records were unobtainable for a sizeable proportion of the population that tended to consult religious healers and traditional health practitioners.¹³ Cancer registry data such as these will therefore under-record prostate cancer because of its clinical and natural history.

While it is possible that the present increasing trend for prostate cancer in Nigeria is real, it may be a result of improved detection from better availability and utilization of health facilities and the ageing population. Environmental factors and race have been cited as significant contributors to the geographic variation in prostate cancer incidence. Cancer of the prostate is presently a frequently occurring cancer in Nigeria and the 15.7% rate of abnormal PSA in men 50 years and older in this study population is cause for concern. It is, therefore, very important to secure histological diagnosis by prostate biopsy and investigate the appropriateness of using 4.0 ng/mL as the cut-off point for PSA abnormality. It will be worthwhile to also investigate the usefulness of 6-month repeat PSA or other tests such as percentage-free prostate-specific antigen as additional screening tools to limit the subpopulation that would require prostate biopsy.^{32,33}

Prostate biopsy is a usual procedure in urology clinics in Nigeria for men who present with prostate pathology.^{26,27,34} Indwelling catheter for urinary retention, transurethral resection and open prostatectomy for BPH, orchidectomy and radical prostatectomy for the management of prostate cancer are well documented in hospital studies.^{5,7,27,35,36} Patients accept prostate biopsy in the hospital setting as part of the management for their

illness for which they sought treatment, most of the time with very severe symptoms and advanced disease. This is contrary to our experience in this community setting, a situation that involves 'healthy' men who did not present with symptoms and do not realize that they may have prostate pathology. This poor response to prostate biopsy that is not specific to this group of Nigerians is bothersome and warrants careful attention.

The men in this study had in-depth group prostate health education by the principal investigator and one-on-one counselling by the clinic doctor about screening for prostate disease and the need for a prostate biopsy in the event of an abnormally high PSA as part of the 'informed consent' process. In addition, the community nurse who hand-delivered results in the form of a health certificate encouraged the men with abnormal results to see the clinic doctor for further counselling regarding their results. The men who presented after receiving their abnormal results were then counselled regarding the necessity and safety of the prostate biopsy procedure. A second home visit was paid to men who were yet to consult the doctor about their abnormal results for the same purpose. Thus, men with abnormal PSA received prostate counselling at least three times and their non-compliance cannot be attributed to lack of knowledge about the procedure. The study surgeon from previous experience with surgical patients noted 'irrational morbid fear of impotence following procedures around the anorectum' as a probably major reason for the default.

The second constraint could be financial as these men pay out-of-pocket for their health and there is no national health insurance scheme in the country. Only 23 (15.2%) work with a company that pays for their medical care. In the three-tier health referral system, patients seen in a primary health center are referred to specialists in the secondary or tertiary health institutions in an urban town. The study, therefore, arranged to reimburse participants for transportation to the teaching hospital and waive the prostate biopsy procedure fee. The study participants, however, had to pay the hospital registration fee so as not to set precedence. It is possible that some of the men could not afford or did not want to spend the time and money required to travel to the teaching hospital for this procedure, as they felt 'healthy'.

Another reason for non-compliance proposed by the clinic doctor is not only fear of the procedure, but more importantly, fear of the diagnosis (cancer fatalism). Fear of the procedure could have been increased because of the emphasis placed on 'all possible risks' of the procedure such as hemorrhage, infection and impotence enumerated on the informed consent as required by the IRB. It is possible that they do not want to take any chances with a procedure in their 'healthy' state. As the study is

not funded to pay for treatment of prostate cancer, inability to pay for treatment in the case of a positive diagnosis can be a true deterrent for having a prostate biopsy, as some people would rather not know about a diagnosis if they cannot afford treatment.

These findings need to be confirmed by a larger study, especially because it is known that African-Americans, who have their origins in Africa, record the highest prostate cancer incidence in the world and previous reports have reported very low rates of prostate cancer in this region. The proposal for extension of the study will include training of the personnel in the local health center to conduct extensive community-based cancer education campaign that will include prostate cancer. The campaign will include audio-visual presentations and question-and-answer discussion sessions with the village council of chiefs and other groups of men and women, the distribution of prostate cancer information materials and in depth personalized discussion sessions at the neighborhood level during home visits by a team that will include a doctor, community nurse and community health worker.

Conclusion

There is a 15.7% prevalence rate of PSA ≥ 4 ng/mL among men 50 years and older in this rural, previously unscreened African population with little or no urbanization or Westernization. This rate is similar to that reported in other previously unscreened populations in developed countries. Although there are several causes of elevated PSA, there is no evidence of prostatitis in this population. Age and enlarged prostate are the main correlates of elevated PSA. This finding, therefore, suggests that prostate cancer may be more common in Sub-Saharan African black men, contrary to earlier reports. The fear of prostate biopsy and of a diagnosis of prostate cancer, irrespective of educational status, is an important finding that deserves careful attention. These findings need to be confirmed in a larger study, and a prostate cancer awareness campaign is required in the area to emphasize the need and safety of prostate biopsy and secure prostate biopsies from the high risk subpopulation with abnormal PSA ≥ 4 ng/mL and/or abnormal prostate on DRE and determine the prevalence of prostate cancer in this population.

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Response to Prostate Biopsy by Nigerian Men: Community and Hospital Experience

**F.A. Ukoli, E. Egbagbe*, F. Akereyeni*, E. Iyamu*, T. Oguike*,
P. Akumabor* and U. Osime***

Department of Surgery, Meharry Medical College, Nashville, TN. U.S.A.

**University of Benin Teaching Hospital, Benin-City, Nigeria*

Summary

Prostate cancer has become the leading male cancer diagnosed in Nigeria, most cases presenting with advanced disease. This study describes determinants of prostate biopsy acceptance after prostate specific antigen (PSA) blood test & digital rectal examination (DRE) in men ≥ 40 yrs. Study response was 84.4% in the community and 63.7% in the hospital, with respective biopsy rates of 3(4.2%) & 57(37.3%), and cancer detection rates of 3(100%) & 43(75%). Mean age was 60.2 ± 13.5 , 365(68.2%) had less than 12 yrs. formal education, 391(81.6%) in the lower economic half. 33(9.6%) community and 111(58.1%) hospital men reported at least one severe urological symptom. Education status, income level, urology symptoms, and symptom severity were not associated with prostate biopsy acceptance. PSA ≥ 100 ngs/ml, and abnormal prostate on DRE were significantly associated with prostate biopsy acceptance. Conclusion: It is proposed that an appropriate prostate cancer control policy and guidelines be developed and used by physicians and urologists. Public awareness should be intensified to increase knowledge and alleviate fear of prostate cancer.

Introduction

The incidence of prostate cancer among Sub-Saharan Africans is about one-fifth that for U.S. blacks, while the lowest rates of 4-7/100,000 are reported from Asian countries¹. African-American blacks record the highest rates in the world, 246/100,000, that is 1.5 times higher than the rate for white Americans.^{2,3} Variation in clinical practice, PSA testing and the use of Transrectal Ultrasonography are important determinants of these trend patterns within

and across nations^{4,5}. In the 1970s Nigerians were three times less likely to have focal prostate cancer than Americans at autopsy⁶, probably a reflection of lower life expectancy. More recently prostate cancer has become the most commonly diagnosed male cancer, estimated incidence of 127/100,000⁷. Most patients present with advanced disease with bone metastasis including paraparesis and/or paraplegia, 2-year survival of 33.0%, and 26.3% dead within six months.⁸⁻¹¹ Histological confirmation was from biopsies collected by digitally-guided prostate biopsy technique.¹¹ PSA test continues to be used for patient follow-up only, even though an appreciable 10.0% prevalence of elevated PSA has been reported¹². This paper reports prostate biopsy acceptance among Southern Nigerian men participating in an IRB approved prostate cancer dietary risk factor study.

Objective

To conduct PSA & DRE screening, refer those with abnormal DRE and/or elevated PSA above 4ngs/dl to the urologist, describe the screening results, and compare the response to prostate biopsy for men recruited from the community and the hospital.

Methods

Men 40 years and older were recruited from two rural, and 2 urban communities in Southern Nigeria by door-to-door invitation¹³, and from two urology clinics of the University of Benin Teaching Hospital, and three general surgery clinics at referring hospitals. Age-eligible participants were provided with study information, informed that participation was voluntary, and refusal will not affect the relationship with their doctor. Interested men went through a complete process of informed consent. Data collected included personal information, urological symptom history, 30mls venous blood, and DRE by a surgeon or urologist. Men with abnormal PSA or DRE results were reviewed by the urologist and prostate biopsy was ordered as appropriate.

Results

450 community-based and 350 hospital-based men were invited to participate in the study with response rates of 355(78.9%) and 204(58.3%) respectively. Mean age was 60.2 ± 13.5 . (See Table 1 for demographic profile). Urological symptoms were reported by 30(15.5%) men <55yrs., 143(52.8%) men 55-74yrs., and 47(60.3%) men ≥75yrs., with a corresponding rate for serious symptoms (retention, incontinence, pain, and haematuria) of 20(10.5%), 93(35.2%), and 30(39.5%), $p < 0.0001$. Urinary frequency, 80(14.7%), pain 76(13.6%), and retention 48(8.8%) were the most common symptoms. 42(7.7%) men reported straining, 41(7.6%) dribbling, 39(7.1%) weak urinary stream, 28(5.1%) urinary incontinence, and 15(2.7%) weak/poor erection. 277(80.8%) men in the community reported no symptoms compared to 37(19.4%) in the hospital, and the respective rate for at least one severe symptom was 33(9.6%) and

Table 1: Demographic Characteristics of Community-Based & Hospital-Based Study Participants

Characteristics	<i>p</i> -value	Recruitment Location		Total	
		Community (N=355)	Hospital (N=204)	N = 559	%
Age Group (yrs.)	<0.0001				
< 45		69 (19.9)	4 (2.0)	73	13.4
45 - 54		101 (29.2)	19 (9.5)	120	22.0
55 - 64		88 (25.4)	56 (28.0)	144	26.4
65 - 74		54 (15.6)	77 (38.5)	131	24.0
75 - 84		25 (7.2)	34 (17.0)	59	10.8
≥ 85		9 (2.6)	10 (5.0)	19	3.5
N/R		9	4	13	
Educational Status	<0.07				
< 6 years		98 (29.0)	56 (28.4)	154	28.8
6 - 11 years		139 (41.1)	72 (36.5)	211	39.4
12 years (Secondary Sch)		45 (13.3)	18 (9.1)	63	11.8
College / Post Secondary		52 (15.4)	45 (22.8)	97	18.1
Post-Graduate		4 (1.2)	6 (3.0)	10	1.9
N/R		17	7	24	
Job Status	<0.0001				
Unemployed		35 (10.1)	15 (7.5)	50	9.1
Employed		252 (72.5)	92 (46.0)	344	62.8
Retired		61 (17.5)	93 (46.5)	154	28.1
N/R		7	4	11	
Occupation	<0.0001				
Unskilled labor		139 (40.3)	57 (30.6)	196	36.9
Semi-Skilled Labor		93 (27.0)	38 (20.4)	131	24.7
Skilled / Service		44 (12.8)	19 (10.2)	63	11.9
Technical / Admn. Support		30 (8.7)	39 (21.0)	69	13.0
Professions/ Snr. Management		39 (11.3)	33 (17.7)	72	13.6
N/R		10	18	28	
Monthly Income	<0.012				
< N25,000		166 (55.3)	121 (67.6)	287	59.9
N25,000 – N44,999		66 (22.0)	38 (21.2)	104	21.7
N45,000 – N84,999		27 (9.0)	8 (4.5)	35	7.3
≥ N85,000		41 (13.7)	12 (6.7)	53	11.1
N/R		55	25	80	
Marital Status	<0.058				
Never Married		7 (2.0)	1 (0.5)	8	1.5
Married		318 (91.6)	183 (92.0)	501	91.8
Divorced		18 (5.2)	7 (3.5)	25	4.6
Widowed		4 (1.2)	8 (4.0)	12	2.2
N/R		8	5	13	
No. of Children	<0.0001				
None		9 (2.6)	3 (1.5)	12	2.2
1 - 8		233 (67.5)	101 (51.3)	334	61.6
9 - 16		84 (24.3)	78 (39.6)	162	29.9
17 – 24		11 (3.2)	13 (6.6)	24	4.4
≥ 25		8 (2.3)	2 (1.0)	10	1.8
N/R		10	7	17	

111(58.1%), $p < 0.0001$ (Table 2). All 18(8.8%) previously diagnosed prostate cancer cases were seen at the hospital, 8(2.9%) in 55-75yrs. age group, and 10(12.3%) in ≥75yrs. age group, $p < 0.0001$.

Table 2: Number, Severity and Duration of Urinary Symptoms & Signs among Community-Based and Hospital-Based Participants

Severity / Duration of Symptoms	Recruitment Location N(%)			p-value
	Community	Hospital	Total	
Symptoms				
None	277 (80.8)	37 (19.4)	314 (58.8)	0.0001
1-3 symptoms	64 (18.7)	115 (60.2)	179 (33.5)	
4-6 symptoms	2 (0.6)	30 (15.7)	32 (6.0)	
≥ 7 symptoms	0 (0.0)	9 (4.7)	9 (1.7)	
Not Recorded	12	13	25	
Symptom Severity				
At least 1 severe	33 (9.6)	111 (58.1)	144 (27.0)	0.0001
No severe + ≥ 3 mild	1 (0.6)	11 (5.8)	12 (2.2)	
No severe + 1 or 2 mild	32 (9.3)	32 (16.8)	64 (12.0)	
Sub-Total	66	154	220	
Duration of Symptoms	N = 66	N = 154	N = 220	
< 2 years	17 (32.7)	107 (69.0)	124 (59.9)	0.0001
2 – 9 years	18 (34.6)	40 (25.8)	58 (28.0)	
≥ 10 years	17 (32.7)	8 (5.2)	25 (12.1)	
N/R	9	4	13	
Sub-Total	66	154	220	
Prostate Examination				
Normal PSA/DRE	222 (62.5)	33 (16.2)	255 (45.6)	0.0001
BPH only	93 (26.2)	36 (17.6)	129 (23.1)	
Elevated PSA/BPH	22 (6.2)	51 (25.0)	73 (13.1)	
Elevated PSA only	11 (3.1)	39 (19.1)	50 (8.9)	
Elevated PSA/Abn. DRE	2 (0.6)	27 (13.2)	29 (5.2)	
DRE suspicious of Cancer	5 (1.4)	18 (8.8)	23 (4.1)	
Prostate Biopsy				
Referred for Biopsy	40 (11.3)	135 (66.2)	175 (31.3)	
Biopsy Done	3 (0.8)	64 (31.4)	67 (12.0)	
Biopsy Acceptance rate	7.5%	47.4%	38.3%	
Cancer Detection rate	100.0%	81.3%	82.1%	

On DRE 115(32.4%) community, and 87(42.7%) hospital men had enlarged prostate, 7(2.0%) to 45(21.1%) abnormal DRE suspicious of prostate cancer, and 35(9.9%) to 117(57.3%) elevated PSA ≥4ngs/ml, $p<0.0001$, respectively. Prostate biopsy was ordered by the urologist for 40(11.3%) community-based, and 135(66.2%) hospital men, 3(0.8%) to 64(31.4%) had the biopsy with corresponding cancer detection rates of 100.0% and 81.3% respectively (Table 2). Biopsy acceptance rates among men with PSA 4.0–20.0ng/ml, 20.1–100.0ngs/ml, and >100.0ngs/ml, were 22.8%, 25.5%, and 80.8% respectively, $p<0.0001$, and for men with normal, enlarged, and abnormal DRE, the rates were 22.4%, 26.0% and 69.2%, $p<0.0001$. Biopsy accept-

Table 3: Pattern of Biopsy Acceptance among Men Referred for Biopsy by DRE and PSA Status in Community-Based and Hospital-Based Participants

Screening Test Result	Biopsy Acceptance Rate Proportion (Rate%)		
	Community	Hospital	Total
PSA ng/ml			
< 4.0	0/5 (0.0%)	8/10 (80.0%)*	8/15 (53.3%)
4.0 – 20.0	2/24 (8.3%)	16/55 (29.1%)	18/79 (22.8%)
20.1 – 100.0	0/10 (0.0%)	12/37 (32.4%)	12/47 (25.5%)
100.1 – 800.0	1/1 (100.0%)	20/25 (80.0%)	21/26 (80.8%)
Total	3/40 (7.5%)	56/127 (44.1%)	59/167 (35.5%)
Prostate Status (DRE)			
Normal	2/11 (18.2%)	9/38 (23.7%)	11/49 (22.4%)
Enlarged	0/22 (0.0%)	19/51 (37.3%)	19/73 (26.0%)
Abnormal (Suspected Cancer)	1/7 (14.3%)	35/46 (76.15)	37/53 (69.2%)
Total	3/40 (7.5%)	64/135 (47.4%)	67/175 (38.3%)

* PSA measured on blood collected after prostate cancer treatment.

ance rate for men with or without pain was respectively 14.3% and 44.3%, $p < 0.001$ (Table 3). Differences in biopsy acceptance by other symptoms, number of symptoms, age group, income level or education status were not significant.

Discussion

As expected, older men and those who were recruited at the hospital clinics had more urological symptoms, higher prevalence of elevated PSA, and higher rates of abnormal DRE suspicious of prostate cancer. Prostate biopsy rate was only 7.5% in the community, lower than the 19.0% in a South African experience in having fewer symptoms was associated with screening refusal¹⁴. In this study symptoms did not influence prostate biopsy acceptance. Cost or lack of health insurance is a recognized barrier to prostate screening¹⁵. In this study biopsy acceptance rate was similar across income groups, and subsidizing biopsy fee did not boost compliance. Either participants could not afford even the subsidized fee, or cost may not be the only constraint. Acceptance was high among men with abnormal DRE or PSA ≥ 100 ngs/ml, regardless of age or socio-economic status. Maybe the urologists focused more on abnormal DRE and very high PSA, and paid less attention to moderately elevated PSA, and PSA that dropped after treating for prostatitis, a very prevalent condition in this population.¹⁶

Lack of knowledge about treatable early stage prostate cancer, as opposed to the more prevalent advanced disease can be a cause for cancer phobia in this population. The fear of cancer, confusion about screening and diagnostic

tests,^{15,17} and the fear of pain and other complications of the prostate biopsy procedure¹⁷ can lead to biopsy refusal. Maybe the rather effective digitally-guided biopsy procedure commonly used in this population¹¹ is less comfortable than the well tolerated ultrasound-guided procedure.^{18,19} Participants may be more influenced by anecdotal experience of other patients, such that prior decision to refuse biopsy was not altered by counseling. Future research should address the attitude of doctors/urologists regarding early detection of prostate cancer by PSA & DRE. The knowledge and attitude of men in the community regarding cancer and surgery in general, and prostate cancer and prostate biopsy in particular should be investigated. Until population studies are completed the true prevalence of prostate cancer in African populations will remain estimates.²⁰⁻²²

Conclusion

There is an urgent need for a prostate cancer discussion at the national, local and institutional levels to generate definite policies and guidelines for early detection. Prostate cancer public awareness campaign through the mass media, complemented by culturally sensitive patient counseling by physicians and urologists is deemed essential. The use of ultrasound-guided prostate biopsy equipment is of utmost priority.

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Anthropometric Body Fat Predictors of Elevated Prostate Specific Antigen among Rural and Urban Nigerians: A Population-Based Study

Flora A. Ukoli¹, Eruke Egbagbe², Barbara B. Zhao¹, Efosa Iyamu², Dale Young⁴, Philip Oside³, Usifo Osime², Lucile L. Adams-Campbell⁴.

- 1 Meharry Medical College, Nashville, TN.
- 2 University of Benin Teaching Hospital, Benin-City, Edo State, Nigeria.
- 3 Specialist Hospital, Warri, Delta State, Nigeria.
- 4 Howard University Cancer Center, Washington DC.

Running Title: Body Fat and Elevated PSA in Nigerians

Key words: Prostate cancer, Elevated PSA, Black men, Central adiposity, WHR, Africa.

Request for reprints should be directed to:

Flora A. M. Ukoli, Department of Surgery, Meharry Medical College,
1005 Dr. D.B. Todd, Jr. Blvd., Nashville, TN 37208

Summary

Background: Obesity has been associated with prostate cancer mortality, but the role of BMI in prostate cancer risk is inconsistent across populations. This study examines the anthropometric body fat correlates of elevated prostate specific antigen ($\text{PSA} \geq 4\text{ng/ml}$) among Nigerians, a low-incidence region, currently reporting a rise in prostate cancer incidence.

Methods: Weight, height and skin fold thickness were measured for men, 40 years and older. Waist-to-hip ratio (WHR) and body mass index (BMI) were computed, obesity defined as $\text{BMI} \geq 30 \text{ kg/m}^2$, prostate examined by digital rectal examination, and blood collected for PSA assay. Mean anthropometry was compared across groups using Student's t-test, Spearman's correlation between anthropometry and the highly skewed PSA, mean PSA tested for linearity across tertiles of all measures, and predictors of PSA determined by multivariate logistic regression controlling for age and enlarged prostate.

Results: Of 350 consecutive men contacted, 281(80.3%) completed the survey, mean age 56.9 ± 13.5 , elevated PSA prevalence 31(11.0%), WHR 0.92 for rural and urban men, BMI (22.9 vs 24.7, $p < 0.002$) and skin fold thickness lower for rural men. PSA correlated directly with age, $r = 0.360$, $p < 0.0001$ and negatively with height, $r = -0.136$, $p < 0.023$. WHR remained a significant predictor of elevated PSA, OR 3.04 (95% CI 1.13 - 8.15), after adjusting for age and enlarged prostate.

Conclusion: Central adiposity (WHR) may be a more important predictor of elevated PSA than BMI. There is need to investigate the role of hormonal, metabolic, genetic and other correlates of central adiposity in prostate cancer risk in this population.

Introduction

Obesity is associated with several diseases such as hypertension, diabetes, heart disease and several forms of cancer including prostate cancer. Obesity has become a serious problem in the United States of America, particularly among the black population (1,2) and is also emerging as an important health risk in African countries such as Nigeria (3), in parallel with prostate cancer, which is now the number one cancer among adult Nigerian men (4). The proportion of all cancers attributable to excess body weight was estimated at 5%, ranging from 2.1% to 8.8% for countries in the European Union, being strongest for cancer of the kidney, gallbladder, colon, endometrium and breast, and 4% for prostate cancer (5). Evidence of increased prostate cancer risk associated with excess body weight has also been reported for white and black men in America (2). Obesity, body mass index (BMI) ≥ 30 kg/m², adjusted for age, was only weakly associated with prostate cancer risk (6), while prostate cancer mortality was significantly higher among obese men (7). Obesity is also associated with higher grade tumors and worse outcome following radical prostatectomy, making the role of obesity in prostate cancer morbidity and mortality particularly important for African Americans who are more likely to be obese than their white counterparts (8).

Studies investigating the role of body fat in the incidence, aggressiveness, and fatality of prostate cancer in different age groups with varying lengths of follow-up have reported inconsistent findings (9). In a case-control study of a very lean Chinese population with mean BMI of 21.9, WHR was associated with clinical prostate cancer with a three-fold increased risk between the lowest and the highest quartile of WHR >0.92 , while adult BMI and pre-adult BMI were not associated with prostate cancer risk (10). A Netherlands cohort study of over 58,000 men did not find any clear association between prostate cancer risk and adult anthropometric parameters, but found an increasing trend for prostate cancer risk for pre-adult BMI, with BMI of 19 as reference (11). The Health Professional Follow-up Study of 33,000 Americans concluded that pre-adult obesity is prospectively related to a lower risk of advanced prostate cancer and that neither adult BMI nor waist and hip circumferences is

appreciably related to prostate cancer risk (12, 13). Case-control (14,15) and cohort (16-20) studies reported BMI as a modest but important anthropometric risk factor for prostate cancer incidence and mortality, and other studies have not found BMI (10-13,21-24), WHR (23,25) or skin fold thickness (26) to predict prostate cancer risk. Pre-adult tallness (12), and adult height (27), are reported as risk factors for aggressive and metastatic prostate cancer, but other studies in the USA (7,28), China (10), and Norway (21) did not support this finding.

African studies have also reported inconsistent relationships between body size and prostate cancer risk. No relationship was found between prostate cancer risk and BMI among Nigerian men described to be of average build and low-normal BMI (4,29). A study from Cameroon reported an association between obesity and prostatic tumor (30), and another of South African blacks alluded to increase in prostate cancer incidence with urbanization and prosperity, with a possible dietary role for Western as compared to Third World diet (31,32). Since anthropometry is an expression of complex interaction of both genetic and environmental factors and a relatively inexpensive method of investigating human body composition (33), this cross-sectional study investigates the anthropometric and body fat correlates and predictors of elevated prostate specific antigen (PSA) 4ng/dl and higher, controlling for enlarged prostate and prostatitis, that can also cause elevated PSA. This is a necessary first step in the investigation of the role of anthropometric body fat indices in prostate cancer risk in this understudied population where prostate cancer cases tend to present in the hospitals with the advanced stage of the disease, invalidating a case-control design. In view of the slow nature of prostate cancer, body fat predictors of prostate cancer risk may not have been impacted sufficiently in the early stages of organ-confined disease to obscure their association with prostate cancer risk. In addition this study will provide feasibility information to develop a cohort study to investigate environmental, dietary and genetic risk factors of prostate cancer from a region with low prostate cancer incidence and differential dietary exposures and obesity rates as their African American peers who share a common genetic ancestry.

Methods

Study population. This study was conducted in two rural and two urban communities in Edo and Delta states of Southern Nigeria. The procedure for recruiting and consenting participants and the process for collecting and processing blood samples have been described (34). A research team made up of a local escort, community health nurse, interviewer and physician visited consecutive houses within the selected communities and requested to speak with men 40 years and older. After introducing themselves and explaining the purpose of the study, interested men received more detail including the process and procedures that will need to be completed. Informed consent documents were read and discussed in detail and only men who then consented by signing the document were recruited. Family members were requested to inform eligible men who were not available at the initial and second planned visits to contact the study team for detailed information if they were interested since the team remained in the community for one year. Of the 350 men contacted, 334(95.4%) consented to participate in the study. Trained interviewers collected general demographic information including history of urinary symptoms, family history of prostate and other cancers at their homes. A trained nurse and interviewer completed anthropometric measurements at the health center with participants wearing light cotton clothes. Weight (WT) was measured in kilograms using a digital scale. Height (HT), waist (WST) at the umbilicus, and hips (HIP) at the highest protrusion of the buttocks with feet together, were measured with a measuring tape in centimeters. Body mass index (BMI) was computed as weight in kilograms divided by height in meters squared, and waist-to-hip ratio (WHR) as waist divided by hips in centimeters. With sleeves rolled up, arm flexed and resting on the chest, mid-arm circumference (MAC), biceps (BI) and triceps (TRI) skin fold thickness of the right arm, and subscapular (SUB) skin fold thickness below the right scapular, were measured in millimeters using the Slim Guide skin fold calipers. The health center physician collected 30ml venous blood into three specimen tubes with a multiple draw vacutainer needle observing all precautions against transmission of blood borne pathogens. The participants then had a digital rectal examination (DRE) by the study

surgeon who has over thirty years of urology experience and they also consulted him regarding problems with urination. The DRE was carried out with a lubricated gloved index finger with the patient lying on their left side with both legs flexed. The prostate size, presence of a sulcus, consistency and nodularity was recorded on a form. The blood samples were centrifuged for 15 minutes after standing for a minimum of 30 minutes. Serum was then pipetted into 2ml. microvials, packed in cardboard storage boxes, and transported on ice within 3 hours of collection to be stored in a laboratory freezer for up to three months until shipment on dry ice to the Howard University laboratory for storage at -70 degrees Celsius. PSA analysis was conducted in a commercial laboratory in the United States of America, using microparticles enzyme immunoassay technology (35). A result slip was distributed by the community health worker to all participants, and men with elevated PSA and/or abnormal DRE were referred by the local health center physician to consult the urologist at the University of Benin Teaching Hospital, Benin-City, after a detailed explanation about the need and safety of the prostate biopsy procedure. The physician contacted non-responders a second time to encourage a visit to the urologist. Those who failed to keep their appointment at the health center were visited at home and advised accordingly by the physician. None of these men reported having a prostate biopsy when contacted two years after the survey, probably because of the fear of possible side effects of this rather invasive procedure of which they are unfamiliar.

Statistical analysis. The statistical program for the social sciences (SPSS 12.0) was used for data collection and basic analysis. The study population was dichotomized by place of residency (rural and urban), occupation (farmers and non-farmers), and age using the cut-point of 55 years, the current age for compulsory public service retirement in Nigeria and the median age of the study population and obesity status defined as $\text{BMI} \geq 30 \text{ kg/m}^2$. Socio-economic status (SES) based on income was stratified to low, medium and high, and educational status to less than 7, 7 –12 and more than 12 years formal education. Mean anthropometry was compared across age, occupation, and residency groups using Student's t-test. Spearman's correlation was used to assess relationship between anthropometry and

PSA, with skewness of 15.68. Mean PSA was tested for linearity across SES and education status, and tertiles of all study anthropometric measurements. The SAS 8.2 program was utilized for multivariate logistic regression to determine the predictors of PSA as a continuous variable and dichotomized as elevated PSA $\geq 4\text{ng/ml}$, controlling for age and enlarged prostate size on (DRE).

Results

Of the 334 men who consented to participate in the study, 281(84.1%) completed the protocol and 53(15.9%) men who did not allow blood draw were excluded from further analysis. Due to scheduling problems at the local health centers, and not self-selection, 23(8.2%) did not have a DRE and 12(3.6%) did not complete anthropometric measurements. There were 178(63.3%) rural and 103(36.7%) urban dwellers with similar age distribution that ranged from 40 –100 years, mean 56.9 ± 13.5 years. Men in the urban community were more educated, 30(30.0%) with more than 12 years formal education as compared to 17(9.6%) rural men and the rates for men with less than 6 years formal education was 9(9.0%) and 79(44.6%) respectively. There were statistically significant differences in their occupational status, 11(11.0%) vs. 130(73.9%) urban and rural men respectively were farmers and 52(50.5%) urban men as compared to 20(11.2%) rural men were retired or not working, $p < 0.0001$. None of the study participants reported a family history of prostate cancer.

The rural men were smaller than their urban counterparts with BMI, 22.9 vs 24.7, $p < 0.001$, obesity rate was 6(3.5%) to 14(14.8%), $p < 0.001$ (Table 1), and all other anthropometric measures were significantly lower in the rural men except WHR that was similar for both groups, 0.92 (Table 2). 3(1.1%) men who had waist ≥ 120 cms. were also obese, and 2 of them were from a rural community.

The prevalence of elevated PSA $\geq 4\text{ng/ml}$ was 13(12.6%) and 18(10.1%) for urban and rural men respectively, but that for enlarged prostate on DRE was significantly higher for urban men, 44(48.9%) vs 52(31.0%). The rates for elevated PSA $\geq 4\text{ng/ml}$ was 30(20.8%) for men ≥ 55 years and 1(0.8%) for those < 55 years. PSA significantly correlated with age only among the older men, $r = 0.29$, $p < 0.0001$. The prevalence of enlarged prostate was statistically higher among older men compared to

the younger men, 74(54.8%) vs 21(17.4%), $p<0.0001$, however the observed rural-urban rate difference for enlarged prostate was significant only for the younger men, 7(8.9%) to 14(33.3%), $p<0.001$, but not for the older men, 44(50.6%) to 30(62.5%).

Older rural men were shorter than the younger ones, 164.8 vs 166.3, and the difference was significant among urban men, 167.2 vs 170.7, $p<0.05$. The older urban men had a higher WHR 0.93 vs 0.91 than their younger counterparts and the similar pattern was significant for rural men, 0.94 vs 0.91, $p<0.0001$. The older farmers were the leanest with BMI of 22.2, MAC 27.9cms but WHR 0.93. The younger farmers had a BMI of 22.9, MAC 29.2cms and WHR 0.90. The younger non-farmers were the middle level workers, low-income artisans and semiskilled workers with a BMI of 23.8, MAC 30.2cms and WHR 0.91. The older non-farmers were the local landlords, contractors and owners of small businesses, with higher BMI of 27, MAC 31.4cms and WHR of 0.97. The prevalence of elevated PSA ≥ 4 ngs/ml was not significantly different for rural and urban men ≥ 55 years, 17(18.9%) vs 13(24.1%) respectively (Table 3), nor for older farmers and non-farmers 16(20.0%) vs. 14(23.0%). Age dichotomized at the median 55 years was a significant predictor of elevated PSA and enlarged prostate, OR 34.74 (95% CI 4.66, 258.75), $p<0.001$ and OR 5.78 (95% CI 3.23, 10.32), $p<0.001$ respectively. The significant anthropometric predictors of elevated PSA were height, OR 0.36 (95% CI 0.16 – 0.82), biceps skin fold, OR 3.04 (95% CI 1.03 – 9.01) and WHR, OR 3.11 (95% CI 1.33 – 7.26). Weight and MAC were negative predictors of enlarged prostate, OR 0.42 (0.25 – 0.71) and OR 0.55 (0.33 – 0.92) (Tables 4). Among men ≥ 55 years only WHR was a significant predictor of elevated PSA, OR 2.67 (95% CI 1.12 – 6.38) while the predictors of enlarged prostate remained as weight and MAC, OR 0.45 (0.23-0.91) and 0.40 (0.20-0.81) respectively (Table not shown). After adjusting for age WHR was a significant predictor of elevated PSA, OR 2.76 (95% CI 1.10, 6.92) and after adjusting for age and enlarged prostate size WHR remained a significant predictor of elevated PSA, OR 3.04 (95% CI 1.13, 8.15) (Table 5). Among men ≥ 55 years WHR was the significant predictor of elevated PSA after adjusting for age, OR 2.62 (95% CI 1.07 – 6.40) and OR 3.00 (95% CI 1.13, 7.94) after adjusting for

both age and enlarged prostate (Table not shown). The incidence of elevated PSA among men in the lowest, middle and third WHR tertiles was 13.5%, 18.0% and 34.9%, $p < 0.0001$. Men in the third WHR tertile recorded increased risk for elevated PSA in comparison to those in the lower WHR tertile with an OR of 3.20 (1.06, 9.64) after adjusting for age and enlarged prostate (Table 6). Waist and skinfold thickness tended to but were not statistical predictors. Obesity defined as $BMI \geq 30$, income and farming occupation did not predict elevated PSA.

Discussion

This community-based study addressed anthropometric prostate cancer risk in apparently healthy Sub-Saharan African men living in Southern Nigeria. The study showed that central adiposity, measured by WHR, not BMI, skin fold thickness, nor height, is associated with risk for elevated PSA. Genetic factors, pre-adult, and adult body fat have consistently been reported to affect prostate cancer risk. However, early life hormonal milieu as expressed in maximum height attained was not found to be an important predictor of increased prostate cancer risk in this study. This is similar to the finding that height alone was not related to prostate cancer deaths in studies conducted in the United States of America (7,28).

Results from case-control and cross-sectional studies show only modest or no association between prostate cancer risk and measures of obesity such as BMI or WHR probably because these measures have already undergone modification either as a result of the disease process or behavior change based on the understanding that weight reduction is beneficial for cancer prognosis. Patients in these studies included those with clinical prostate cancer (18), prostate cancer stage T2 and greater (23) and aggressive prostate cancer (10). Some cohort studies recruited and followed patients for several years after diagnosis as reflected in the person-years reported (19).

Cohort studies that recorded anthropometry before the onset of disease did show obesity, BMI, height and other aspects of body size to be risk factors for prostate cancer incidence and mortality, especially when measurements were collected as part of a study protocol by trained staff. (7,16,20).

That the association between body size and prostate cancer risk is stronger for those who were diagnosed eleven years after the study was initiated underscores the importance of studying baseline measures long before the onset of disease, before the disease process begins to modify body fat (36). Cohort studies where the mean age of participants at recruitment was over 65 years might have failed to demonstrate any association between measures of obesity and prostate cancer for the same reason (13). Pre-adult BMI provided a better alternative to adult BMI except that it is more related to lean body mass than obesity. (11,21). This study evaluated the anthropometric correlates and predictors of elevated PSA. The neoplastic process, if present in the pre-diagnostic or latent stages may not have appreciably impacted physical measurements, as none of the participants presented with overt disease, nor reported weight loss within the past 12 months.

Epidemiological studies that relied on self-reported physical measurements, or information from multi-center routine clinical settings (24), may lack the accuracy of research protocols, leading to possible distortion of the association between such measures and disease risk. Since waist and hip measurements are not routinely collected, many studies lacked information on pre-adult or adult WHR (11,21), a measurement that this study was able to collect.

Since age and prostate enlargement are the strongest correlates of elevated PSA, the odds ratio for the anthropometric and other predictors of prostate cancer were adjusted for both variables. Since benign prostatic hyperplasia does not preclude the risk for prostate cancer, analysis was combined for all men regardless of prostate size. Central adiposity, not BMI or skin fold thickness, was associated with the risk for elevated PSA in this population. The confounding role of diet and hormones in cancer etiology cannot be over emphasized (37).

Young men from low socio-economic status (SES) and older men retiring from very low-pay city jobs remain in the rural setting as peasant farmers. Lack of occupation related physical activity among young urban men was reflected in high BMI in comparison with their rural counterparts and older urban men recorded the highest BMI, evidence of their more affluent and leisurely lifestyle.

Physical inactivity and diet are documented important cancer risk factors (38,39) that have not been directly addressed in this study, so farming was used as a proxy measure of physical activity. Cross stratification by farming status and age cut-point 55 years provided four cohorts with differential past and present nutrition, physical activity and physical growth history. BMI runs a continuum with the older farmers having the lowest measure, followed by young farmers, the young non-farmers, and the older non-farmers, who had the highest BMI. Older farmers with past and present high levels of physical activity recorded similar prevalence of elevated PSA as their non-farmer peers who lacked physical activity. Although the pattern of BMI was different for both groups of men, WHR and the prevalence of elevated PSA were similar. It would appear that the risk for elevated PSA associated more with central adiposity (WHR), rather than BMI, and the effect was not attenuated by a history of physical activity. This study did not record pre-adult BMI / obesity, a factor that has been reported to be a risk for prostate cancer (11,40,41).

That central adiposity predicts prostate cancer risk in such a lean population with low prostate cancer incidence is serious implication for populations with high prevalence of obesity and prostate cancer, especially as severe obesity has been reported to explain the relative disadvantage in prostate and breast cancer outcomes for African Americans (8,42). African American men record increasing prevalence of overweight, from 53.9% in 1960 to 71.3% in 2000 (43) and a higher incidence of prostate cancer than their white counterparts at 275.9/100,000 (44). Thus further research into the metabolic and hormonal mechanisms of prostate cancer etiology in blacks both in Africa and America is necessary so as to include a wider range of body size, nutrient exposures, and genetic admixture.

This study is limited by small sample size and the lack of prostate biopsy information on the men with elevated PSA. It confirms the feasibility of large community-based prostate cancer cohort study with recruitment sites in Nigeria. The study strengths include the fact that physical measurements not routinely collected have been included in the protocol, and that measurements were made before the onset of overt disease. A follow-up study can be designed to facilitate and encourage

prostate biopsy in this population, identify men who subsequently become diagnosed with prostate cancer and evaluate the anthropometric predictors of prostate cancer retrospectively. The fact that none of the study participants reported a family history of prostate cancer may be as a result of general lack of awareness of the disease, inattention to pathological cause of death, dying with undiagnosed prostate cancer, very low incidence of the disease in the previous generation, or a combination of factors. This population provides a unique opportunity to prospectively study the anthropometric, metabolic, hormonal and genetic predictors of prostate cancer in a designated low-incidence region, provide data to estimate the true incidence of the disease in the region, and recruit families with multiple cases of prostate cancer for more detailed genetic studies.

Conclusion

The prevalence of elevated PSA ≥ 4.0 ng/ml was 11.0% among rural and urban Africans with an obesity rate of 8%, and this risk was predicted by central adiposity (WHR), but not by BMI), and was not attenuated by a history of increased physical activity. This is consistent with the current implication of hormonal or insulin-related mechanism in the etiology of prostate cancer. There is an urgent need to increase prostate cancer awareness, and to facilitate a positive attitude to prostate biopsy among those with elevated PSA. Socio-economically stratified cohorts with differential body size patterns, dietary, and physical activity history have been identified and can be followed up in a cohort study that will collect body fat measurement by the impedance technique, hormonal and metabolic correlates of central obesity, dietary and physical activity information, and genetic data to determine their interactions in the pathogenesis of prostate cancer.

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Table 1: Comparison between Rural and Urban Nigerian Men in their Distribution of Demographic Characteristics, PSA and Prostate Size

Characteristics	RURAL 178 (63.3%)	URBAN 103 (36.7%)	TOTAL N=281		p-val *
			N	%	
Age					ns
< 45	38(21.7)	18(17.6)	56	20.2	
45-54	47(26.9)	30(29.4)	77	27.8	
55-64	43(24.6)	26(25.5)	69	24.9	
65-74	29(16.6)	17(16.7)	46	16.6	
75-84	12(6.9)	9(8.8)	21	7.6	
≥85	6(3.4)	2(2.0)	8	2.9	
Not Recorded	3 --	1 --	4	--	
Mean Age	56.7 ± 14.1	57.4 ± 12.5	56.9 ± 13.5		
Education					<0.0001
< 6 years	79(44.6)	9(9.0)	88	31.8	
6 – 12 years	81(45.8)	61(61.0)	142	51.3	
> 12 years	17(9.6)	30(30.0)	47	17.0	
Not Recorded	1 --	3 --	4	--	
Occupation					<0.0001
Farming	130(73.9)	11(11.0)	141	51.1	
Semi-/Skilled	20(11.4)	38(38.0)	58	21.0	
Teaching/Jr.Admin	22(12.5)	34(34.0)	56	20.3	
Manager/Professional	4(2.3)	17(17.0)	21	7.6	
Not Recorded	2 --	3 --	5	--	
PSA (ng/ml)					ns
0 - 2.4	143(80.3)	83(80.6)	226	80.4	
2.5 - 3.9	17(9.6)	7(6.8)	24	8.5	
4.0 - 9.9	6(3.4)	7(6.8)	13	4.6	
10.0-49.9	11(6.2)	3(2.9)	14	5.0	
≥ 50.0	1(0.6)	3(2.9)	4	1.4	
Prostate Size					<0.007
Normal	116(69.0)	46(51.1)	162	57.7	
Enlarged	52(31.0)	44(48.9)	96	34.1	
Not Done	10 --	13 --	23	--	
Obesity (BMI)**					<0.001
Underweight	17(9.8)	3(3.2)	20	7.4	
Normal	113(64.9)	49(51.6)	162	60.2	
Overweight	38(21.8)	29(30.5)	67	24.9	
Obese Class I	5(2.9)	11(11.6)	16	5.9	
Obese Class II	1(0.6)	3(3.2)	4	0.5	
Not recorded	4 --	8 --	12	--	

* p-values for comparison between rural and urban distributions.

** Underweight = BMI < 18.5; Normal = BMI 18.5-24.9; Overweight = BMI 25.0-29.9; Obese class I = BMI 30.0 –34.9; Obese class II = BMI 35.0-39.9; Extreme Obesity = BMI ≥40.

Table 2: Mean and Median Anthropometric Measurements of Rural and Urban Nigerian Men

Measurements	Rural	Mean Urban	Rural	Median Urban	p-val
WST (cms.)	83.5	87.9	81.4	87.5	.000
HIP (cms.)	90.1	95.6	89	95.2	.000
MAC (cms.)	28.2	29.3	28.1	29.1	.005
HT (cms.)	165.6	168.9	165.5	168.2	.001
WT (kgs.)	62.9	70.7	61.0	69.2	.000
BI (mms.)	4.7	6.0	4.0	5.0	.000
TRI (mms.)	7.6	10.9	7.0	10.0	.000
SUB (mms.)	12.1	15.7	11.0	15.0	.000
BTS (mms.)	8.2	10.9	7.0	10.3	.000
BMI	22.9	24.7	22.5	23.8	.002
WHR	0.92	0.92	0.92	0.92	0.38
PSA >= 4ng/ml	18(10.1%)	13(12.6%)			0.32

Table 3 Comparison of Mean Anthropometric Measurements and Incidence of Elevated PSA by Age Cohort for Rural and Urban Nigerians

Measures	Mean (sd)			
	Rural		Urban	
	<55 n=85	>=55 n=90	<55 n=48	>=55 n=54
Waist (cm)	81.9 (10.1)	84.8 (11.9)	85.9 (9.8)	89.5 (11.3)
Hip (cm)	90.2 (8.1)	90.1 (9.3)	94.8 (7.7)	96.1 (9.3)
MAC (cm)	28.5 (3.2)	28.0 (3.1)	29.3 (3.3)	29.3 (3.6)
Height (cm)	166.3 (6.8)	164.8 (6.7)	170.7 (7.6)	167.2 (8.2) *
Weight (kg)	63.3 (10.8)	62.3 (12.1)	71.0 (13.0)	69.8 (15.0)
Biceps (mm)	4.5 (2.1)	5.0 (2.7)	5.6 (2.8)	6.3 (2.7)
Triceps (mm)	7.1 (3.0)	8.2 (3.7)	10.5 (5.5)	11.0 (4.4)
Subscapular (mm)	11.7 (4.9)	12.6 (5.7)	14.9 (6.9)	16.4 (7.0)
BMI	22.9 (3.6)	22.9 (3.9)	24.4 (4.2)	25.0 (4.8)
WHR	0.91 (0.07)	0.94 (0.06) ***	0.91 (.07)	0.93 (.06)
Age	45.4 (4.3)	67.2 (11.6)	46.7 (4.3)	67.0 (9.1)
% Elevated PSA	1(1.2%)	17(18.9%)* **	0(0%)	13(24.1%)* **

* p < 0.05

** p < 0.001

*** p < 0.0001

Table 4. Anthropometric predictors of elevated PSA and enlarged prostate in Nigerian men.

Predictors	Mean (Standard Deviation)		Crude Odds Ratio (95% CI)	
	Elevated PSA	Normal PSA	Elevated PSA	Enlarged Prostate
Weight	66.19 (19.59)	65.61 (12.06)	0.72 (0.34, 1.55)	0.42 (0.25, 0.71) ***
Height	165.41 (7.30)	166.95 (7.48)	0.36 (0.16, 0.82)**	0.94 (0.57, 1.57)
Waist	89.25 (14.32)	84.56 (10.64)	1.15 (0.54, 2.46)	1.21 (0.73, 2.02)
Hip	93.07 (11.64)	91.97 (8.73)	0.98 (0.46, 2.08)	0.76 (0.46, 1.28)
MAC	28.53 (4.24)	28.64 (3.18)	0.68 (0.32, 1.46)	0.55 (0.33, 0.92) *
Bicep	5.97 (3.11)	5.07 (2.55)	3.04 (1.03, 9.01) *	1.52 (0.84, 2.72)
Tricep	10.18 (4.66)	8.63 (4.31)	1.61 (0.75, 3.47)	1.14 (0.68, 1.92)
Subscapular	15.00 (7.75)	13.24 (5.95)	1.53 (0.71, 3.29)	1.03 (0.61, 1.73)
BMI	23.96 (5.52)	23.51 (3.86)	0.74 (0.34, 1.59)	0.82 (0.49, 1.36)
WHR	0.95 (0.63)	0.92 (0.65)	3.11 (1.33, 7.26) **	1.45 (0.87, 2.43)
*** p < 0.001 ** p < 0.01 * p < 0.05				

Table 5. Anthropometric predictors of elevated PSA among Nigerian men:
Odds Ratio adjusted for age and enlarged prostate.

Predictors	Crude Odds Ratio (95% CI)	
	OR Adjusted for Age	OR Adjusted for Age and Enlarged Prostate
Weight	1.03 (0.44,2.39)	1.15 (0.45,2.89)
Height	0.45 (0.19, 1.08)	0.56 (0.22, 1.39)
Waist	1.36 (0.59, 3.16)	1.01 (0.41, 2.45)
Hip	1.04 (0.45, 2.39)	1.14 (0.47, 2.78)
MAC	0.90 (0.39, 2.08)	1.19 (0.48, 2.98)
Bicep	3.04 (0.85,10.9)	2.97 (0.77,11.5)
Tricep	1.73 (0.73, 4.09)	1.62 (0.65,4.03)
Subscapular	1.74 (0.73, 4.13)	1.47 (0.59, 3.65)
BMI	1.00 (0.43, 2.31)	0.86 (0.35, 2.13)
WHR	2.76 (1.10, 6.92) **	3.04 (1.13, 8.15) **

** p < 0.01

Table 6: Waist-Hip-Ratio and other Categorical Predictors of Elevated PSA among Nigerians: Odds Ratio Adjusted for Age and Enlarged Prostate.

Predictor	Cases (Elevated PSA)	Controls (Normal PSA)	Odds Ratio	95% CI	p-val
Age					
< 65	13 (41.9)	189 (76.8)	1.00		
≥ 65	18 (58.1)	57 (23.2)	4.59	2.12, 9.94	0.0001
Waist-hip-ratio					
0.66 – 0.90	6 (20.0)	89 (36.6)	1.00		
0.90 – 0.95	8 (26.7)	88 (36.2)	1.15	0.31, 4.22	0.43
0.95 – 1.17	16 (53.3)	66 (27.2)	3.20	1.06, 9.64	0.02
Obesity (BMI > 30)					
No	14 (56.0)	148 (66.1)	1.00		
Yes	11 (44.0)	76 (33.9)	1.53	0.66, 3.53	0.32
Income					
Low	21 (77.8)	146 (65.8)	1.00		
Medium	1 (3.7)	40 (18.0)	0.40	0.05, 3.42	0.25
High	5 (18.5)	36 (16.2)	2.01	0.71, 5.70	0.10
Occupation					
All Others	14 (45.2)	121 (49.4)	1.00		
Farming	17 (54.8)	124 (50.6)	0.72	0.29, 1.78	0.66

Roots of Prostate Cancer in African-American Men

Folakemi T. Odedina, PhD; J. Olufemi Ogunbiyi, MBBS, FWACP (Lab Med); and
Flora A.M. Ukoli, MBBS, DPH, MPH

Tallahassee, Florida; Ibadan, Nigeria; and Nashville, Tennessee

To fully understand the role of genetics and environment (biotic, abiotic and sociocultural) in the prostate cancer disparity experienced by African-American men, this paper examined the rates of prostate cancer among African-American men and one of their ancestral populations in west Africa. Data sources were from the World Health Organization (WHO) and reported hospital records in the literature. Based on the WHO's worldwide cancer data, west African men have much lower prostate cancer incidence and mortality compared to African-American men. For example, compared to Nigerian men, African-American men are >10 times likely to develop prostate cancer and 3.5 times likely to die from the disease. However, contrary to the global ranking by WHO, there is documented evidence in the literature indicating that prostate cancer in at least one west African country is similar to rates found in the United States and in Caribbean Islands. To better address prostate cancer disparity, future studies should study populations and subgroups from central and west Africa, the original source population for African Americans.

Key words: prostate cancer ■ African Americans ■ men's health

The report of the Descriptive Epidemiology Group of the International Agency for Research on Cancer (IARC)¹ presents estimates of the incidence and prevalence of and mortality from 27 cancers for all countries in the world. The report estimated that in 2002, prostate cancer ranked first for the five-year prevalent cases of all cancers among men in the world. There were 2,368,669 reported cases. Prostate cancer ranked second among men for new cancer cases for all ages worldwide. In the United States, the 2005 cancer morbidity and mortality estimates by the American Cancer Society² indicate that prostate cancer will continue to lead the new cancer cases and will be the second leading cause of cancer deaths in men. Among men, it is estimated that 232,090 new prostate cancer cases and 30,350 prostate cancer deaths will be reported in 2005.² Although prostate cancer affects men regardless of their racial group, a disproportionate burden is experienced by African-American men. African-American men are 2.4 times more likely to die of prostate cancer compared with white men.² They also have the highest incidence of prostate cancer compared to other racial/ethnic groups in the United States.

The worldwide differences in the incidence of prostate cancer and the noticeable variations among ethnic groups are noted by Gronberg³ to be caused by multiple factors, including genetic susceptibility, external risk factors, health differences and cancer registration. A comprehensive understanding of the reason(s) for the ethnic variations in prostate cancer morbidity and mortality within the United States remains elusive. This ethnic variation has even been found to persist when dietary and lifestyle factors were accounted for among men of similar educational level.⁴ An important question that needs to be answered is: Does this prostate cancer disparity also exist among the original source population for African Americans? In this paper, we examined the prostate cancer burden experienced by one of the ancestral populations of African Americans in attempt to understand the prostate cancer disparity experienced by African-American men.

© 2006. From The Economic, Social & Administrative Pharmacy Division (Odedina, professor and division director) and Florida A&M University Center for Minority Prostate Cancer Training & Research, Florida A&M University College of Pharmacy & Pharmaceutical Sciences, Tallahassee, FL (Odedina, program director); Department of Pathology (anatomic pathology), University College Hospital, Ibadan, Nigeria (Ogunbiyi, professor); and Prostate Cancer Research Program, Department of Surgery, Meharry Medical College, Department of Surgery, Nashville, TN (Ukoli, associate professor). Send correspondence and reprint requests for *J Natl Med Assoc.* 2006;98:xxx-xxx to: Dr. Folakemi T. Odedina, Suite 200, Dyson Pharmacy Building, Florida A&M University Economic, Social and Administrative Pharmacy Division, Tallahassee, FL 32307; e-mail: folakemi.odedina@famuedu

The Ancestral Group of African Americans

African Americans are blacks of African origin living in the United States. The forefathers of African Americans were originally taken from Africa as slaves. From the transatlantic slave trade between 1450 and 1900,⁵ the number of Africans imported to Americas was up to five times that of Africans imported to Europe. Most of the slaves arrived in Brazil, Spanish Empire, British West Indies and French West Indies. Only 4.4% of the slaves ended up in British North America and the United States.⁵ The African regions where slaves were mainly sourced for the transatlantic slave trade were Senegambia, Upper Guinea, Windward Coast, Gold Coast, Bight of Benin, Bight of Biafra, west central and southeast.⁶

Over 10 million slaves were exported between 1650 and 1900. The majority of the transatlantic slaves were from Bight of Benin and Bight of Biafra. These two regions, approximated to be the country Nigeria,⁷⁻⁹ alone supplied about 3.5 million slaves, constituting about 35% of the slaves. Other countries representing the regions of the slave trade are Senegal-Gambia, Sierra Leone, Ivory Coast, Ghana and Cameroon–North Angola.

Since the slave trade, African Americans, through intermarriage and interbreeding with Native Americans and Europeans of diverse ethnic backgrounds, have gene pools that are more heterogeneous.^{10,11} However, being the primary source population for

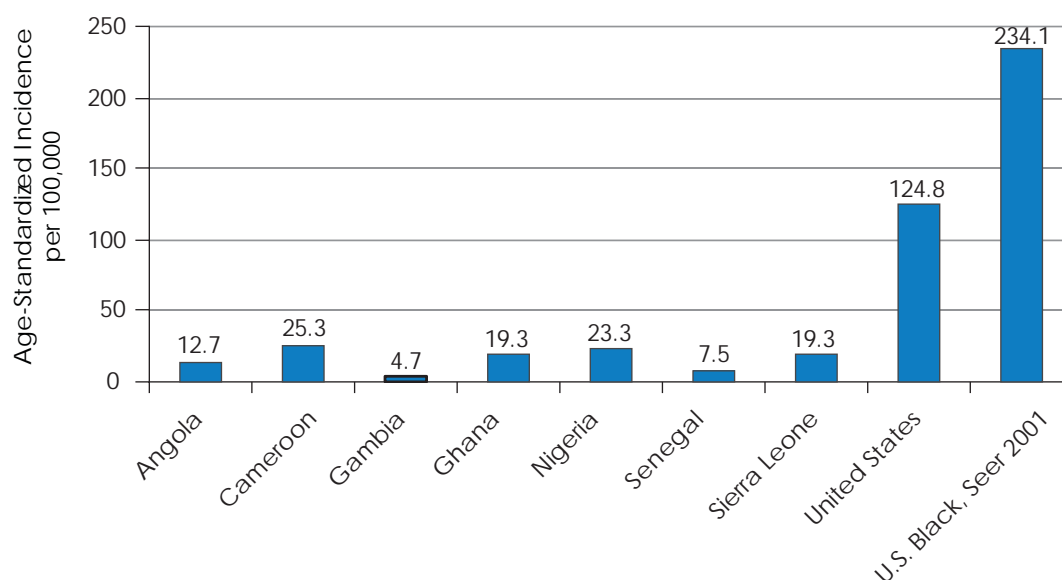
African Americans, central and west Africans share similar genetic structure with African Americans. Below we explore the concept that this shared genetic structure may be one of the factors responsible for the ethnic differences in prostate cancer risk.

Prostate Cancer Incidence and Mortality among Ancestral Groups of African Americans Compared with African Americans

Prostate cancer morbidity and mortality rates vary worldwide among diverse groups. In general, the more developed regions have higher morbidity and mortality rates compared with less developed regions.¹ In 2002, the United States was documented as having the highest prostate cancer incidence (124.8), while Barbados led in prostate cancer mortality (55.3).¹ Worldwide prostate cancer statistics for African men in Nigeria, Senegal, Gambia, Sierra Leone, Ivory Coast, Ghana, Cameroon and Angola provide an interesting observation compared to African-American men (Figures 1 and 2). The reported prostate cancer incidence and mortality for the ancestral relatives of African Americans are very low. For example, compared to Nigerians, African Americans are >10 times likely to develop prostate cancer and 3.5 times likely to die from the disease.

Based on the worldwide comparison,¹ can we conclude that prostate cancer incidence among African-American men in the United States is higher than that

Figure 1. Age-standardized incidence rates for prostate cancer



Source: Ferlay J, Bray F, Pisani P, and Parkin DM. GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide. IARC CancerBase No. 5, version 2.0, IARC Press, Lyon, 2004

seen in other black men sharing the same genetic characteristic? If this is the case, it indicates that environmental conditions and/or the lifestyle of African-American men may be major factors responsible for the prostate cancer disparities experienced by this group. We propose that the true prostate cancer rates for west Africans may be underestimated by IARC,¹ since there are no data available on cancer incidence and mortality for most of the west African countries. For example, the cancer incidence rates for 16 countries in western Africa was based on unweighted averages of Guinea, Conakry (1996–1999), Gambia (1997–1998), Mali, Bamako (1993–1997), Niger and Niamey (1993–1999).¹ In cases where the cancer incidence rates for a country are not available, the method of cancer data estimation by IARC is based on data provided from select cities in the country and/or regional data. Thus, the international cancer rates published by IARC¹ depend on the degree of detail and accuracy of the data available for each country.

The reported difference in prostate cancer burden among Africans has been attributed to several factors, including underreporting,¹² lack of appropriate diagnosis,¹²⁻¹⁵ limited access to care,¹³ differences in technical manpower and infrastructure,¹³ and the quality of cancer data systems.^{13,16-19} Especially important is the quality of the data from cancer registries in Africa. Direct comparisons of the prostate cancer burden experienced by African-American men to that of their African ancestral relatives cannot be done if there are differences in the data reporting methods for incidence and prevalence of

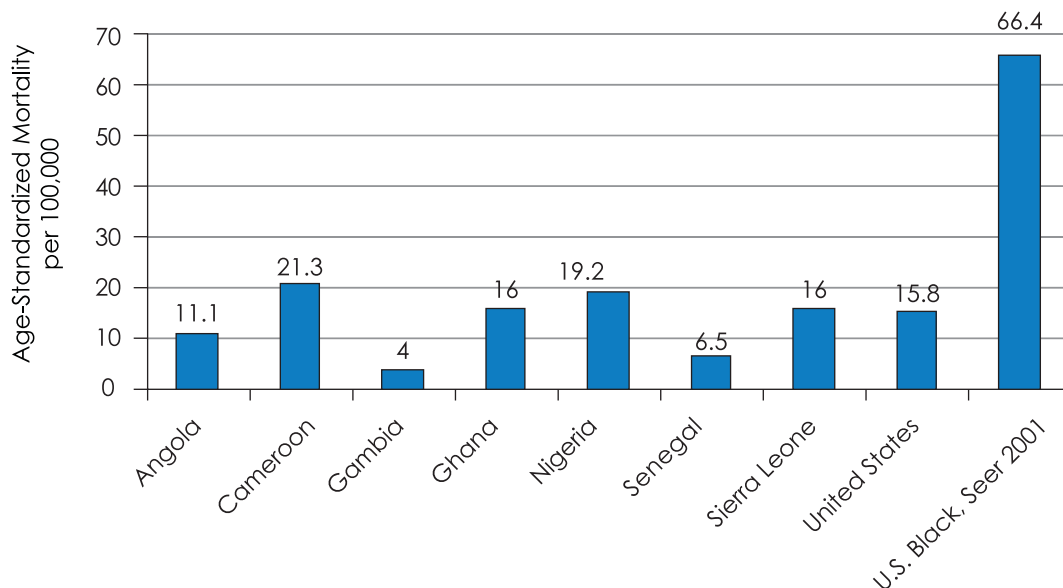
and mortality from prostate cancer.

Cancer registries make it possible to delineate public health priorities as well as plan and monitor comprehensive strategies for cancer control. However, as specified by the International Association of Cancer Registries, “The comparative value of the statistics which cancer registries produce depends upon the use of common methods, and definitions, so that international collaboration in this area has a very important role.”²⁰ For valid comparisons among African-American men and their descendants from different countries, the definitions for collecting, coding and presenting data have to be comparable among registries. In the absence of a viable cancer registration system that allows comparison of population-based information on prostate cancer incidence and outcome, it cannot be concluded that prostate cancer burden among African-American men is significantly higher than that of their ancestral groups. A close review of the ancestral group that has significant genetic ties to African Americans, i.e., Nigerians, provides an insight on possible relative contribution of genetics as a risk factor for prostate cancer.

Prostate Cancer Burden in West Africa: Case Analysis of Nigeria

African-American men have the highest incidence of prostate cancer in the United States,² and African Caribbean men have the highest rate of prostate cancer in the world.²¹ The high risk of prostate cancer in these groups (both of west African descent) suggests that west African men are likely to also have a high

Figure 2. Age-standardized mortality rates for prostate cancer¹



Source: Ferlay J, Bray F, Pisani P, et al. GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide. IARC CancerBase No. 5, version 2.0, IARC Press, Lyon, 2004

incidence of prostate cancer. The 2002 age-standardized prostate cancer incidence rate estimated for Nigeria, the most populous country in west Africa, was 23.3.¹ Presently, there is no national cancer registry in Nigeria to accurately document prostate cancer burden in Nigerian men. However, contrary to the global rankings by the World Health Organization, several studies indicate higher incidence of prostate cancer in Nigerian men.^{12,14,22-33} These findings directly conflict with global rankings of low prostate cancer risk for Nigerian men.

As early as 1981, Udeh,²² in a 10-year retrospective study of prostate carcinoma in Nigeria, reported an increasing incidence of prostate cancer among Nigerians. Also, Lawani et al.,²³ conducted a 20-year review of the genitourinary tract tumors in Ibadan, a populous city in Nigeria, and concluded that prostate cancer was the most common urological cancer in Ibadan. Reports of high incidence of prostate cancer have also been found in Lagos²⁴ and Benin,²⁵ two other cities in Nigeria. By the late 1990s, it was apparent that the global report of low prostate cancer incidence among Nigerian men was an underestimation. In a prospective study, Osegbe²⁶ investigated the validity of the prostate cancer global ranking for Nigerian men studying men age ≥ 45 years with prostatic symptoms. Osegbe found the hospital incidence rate to be 127 per 100,000 cases, concluding that prostate cancer rate among Nigerian men may be as great as the rate seen in African-American men. In another study, Ogunbiyi and Shittu¹⁴ used the Ibadan Cancer Registry to show a high incidence of prostate cancer among Nigerian men. Comparing 1980–1988 and 1989–1996 registry data, the authors found prostate cancer to constitute 11% of all male cancers, ranking first among all cancers in Nigerian men.

Recent studies continue to support the evidence of high prostate cancer risk among Nigerians. Eke and Sapira,²⁷ in a 14-year retrospective study of prostate cancer patients in Port Harcourt, reported a hospital incidence of 114 per 100,000. Nwofor and Oranusi²⁸ also investigated prostate cancer patients between the ages of 44–92 in Nnewi, Nigeria. In the five-year retrospective study, prostate cancer was found to constitute 77% of all urological cancer, making it the most common urological cancer among Nnewi men. In agreement with these studies, other prostate cancer investigations have found high prostate cancer risk in different regions of Nigeria, including the north,^{29,30} southeast,^{31,32} west,³³⁻³⁶ and the rural south.¹²

Understanding Prostate Cancer Disparity

Prostate cancer occurs all over the world, while the prevalence of the aggressive forms of prostate

cancer vary³⁴⁻³⁷ with significant burden for African-American men. Understanding the primary reasons for the prostate cancer disparity experienced by African-American men is essential for successful intervention programs to eliminate this disparity. Available evidence seems to indicate that this disparity may be shared by other black men of African descent, especially those with origins from west Africa. Unfortunately, the cancer data available in most African countries do not permit valid global comparisons of prostate cancer incidence and mortality. Thus, at this time there is no conclusive evidence on prostate cancer risk in African black men. There are more questions than answers: What is responsible for the high prostate cancer burden among African-American men? Is the disparate burden in African-American men present in the source population, i.e., indigenous west and central African men? Does the similar genetic characteristic of black men of west and central African ancestry put them at higher risk for prostate cancer compared with other groups? Or are there common environmental conditions/lifestyle factors among these men that may be responsible for the prostate cancer burden experienced by this group? What is the relative contribution of genetic, lifestyle and environmental factors in prostate cancer incidence and mortality among this group?

Next Steps

African-American men continue to experience a significant burden of prostate cancer compared to other ethnic groups in the United States. At first glance, the high rates of prostate cancer incidence and mortality reported among black men in the Caribbean Islands, as well as the increasing evidence of high prostate cancer burden among Nigerians, may suggest strong influence of genetics. However, only about 5–10% of prostate cancer cases have been linked to high-risk inherited genetic factors or prostate cancer susceptibility genes.³⁸ With the realization that biotic, abiotic and sociocultural environmental factors also affect the development and progression of prostate cancer,^{3,39} it is necessary to confirm shared environmental factors that may also predispose African-American men and their ancestral relatives to prostate cancer.

To fully understand the role of environment and genetics in prostate cancer disparity as well as to begin to successfully address this disparity, more studies need to be conducted among indigenous west and central Africans. From the case analysis of Nigeria, it appears that the incidence rates based on hospital series data may be similar to rates in the United States data for African-American men. Future studies should focus on comparisons of

prostate cancer risk factors among black men of similar ancestral origin to African Americans.

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Original article

Prostate cancer screening between low-income African-American and Caucasian men[☆]

Jay H. Fowke, Ph.D., M.P.H.^{a,*}, David Schlundt, Ph.D.^b, Lisa B. Signorello, Sc.D.^{a,c},
Flora A.M. Ukoli, M.B.B.S., M.P.H.^d, William J. Blot, Ph.D.^{a,c}

^a Vanderbilt-Ingram Cancer Center, Vanderbilt University, Nashville, TN 37232, USA

^b Department of Psychology, Vanderbilt University, Nashville, TN 37235, USA

^c International Epidemiology Institute, Rockville, MD 20850, USA

^d Department of Surgery, Meharry Medical College, Nashville, TN 37208, USA

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Abstract

Objective: African-Americans (AA) are more likely than Caucasians (CA) to be diagnosed with advanced prostate cancer, perhaps due to delayed detection. We investigated racial differences in prostate cancer screening according to age and socioeconomic and demographic indices in a large and predominantly low-income population.

Methods: In-person interviews were conducted with 12,552 men, 84% AA, recruited during 2002 through 2004 from 25 community health centers in the southern United States. Prostate specific antigen test (PSA) and digital rectal examination (DRE) histories, and socioeconomic and demographic indices (i.e., education, household income, health insurance, and marital status) were determined. Odds ratios (OR) from logistic regression summarized the screening and race association as a function of age, while controlling for socioeconomic status (SES).

Results: Racial differences in screening prevalence varied with age. Of men older than 65 years, CA were significantly more likely to report a PSA test (OR = 1.4) or DRE (OR = 1.5) within the past 12 months. However, these disparities were reduced with control for SES (PSA: OR = 1.2; DRE: OR = 1.3, $P > 0.05$). In contrast, at ages younger than 65, CA were equally or less likely to have received a recent PSA test or DRE, particularly at ages 45–49 years (PSA: OR = 0.7; DRE: OR = 0.9), with little change after SES adjustment.

Conclusions: Consistent with several screening recommendations, younger AA men, especially those younger than age 50, are more likely than CA to have had a recent PSA test or DRE, independent of SES. Of men older than age 65, less frequent use of screening among AA than CA seems partly attributable to SES and factors other than race. © 2005 Elsevier Inc. All rights reserved.

Keywords: Prostate cancer; Prostate specific antigen; Screening; Race; Socioeconomic status

1. Introduction

Race remains a consistent risk factor for prostate cancer incidence and mortality among U.S. men. African-American (AA) men have a higher incidence and are diagnosed with more advanced cancer compared to Caucasian (CA) men, and prostate cancer mortality is approximately 2-fold greater [1–5]. Genetic [6,7] or lifestyle factors [8,9] may initiate or promote prostate tumors preferentially among AA men. However, epidemiologic, genetic, and endocrine in-

vestigations attempting to identify a biologic or lifestyle rationale to explain this disparity have been inconclusive.

Almost all prostate cancer diagnoses in the United States now are in response to a positive prostate cancer-screening test. The prostate specific antigen (PSA) test and digital rectal examination (DRE) enable the detection of early-stage and organ-confined disease among otherwise asymptomatic men. Prior community-based or registry-based studies have found that AA men were less knowledgeable about prostate cancer screening tests [10,11] and less likely to be screened than CA men [12–14], suggesting that delayed or inconsistent administration of screening procedures may contribute to late-stage prostate cancer detection among AA men.

Screening has not been conclusively shown to reduce mor-

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* Corresponding author. Tel.: +1-615-936-2903; fax: +1-615-936-1269.

E-mail address: jay.fowke@vanderbilt.edu (J.H. Fowke).

tality, and aggressive promotion of prostate screening is controversial. Nevertheless, the American Cancer Society (ACS) and other groups have created age and race-specific guidelines recommending annual consultation and screening offered to CA men beginning at age 50 and to AA and high-risk men beginning at age 45. However, implementation of screening guidelines may be influenced by socioeconomic factors and health care access [10,12,15]. Men living in low-income and low-education census tracts, men without health insurance, or men with publicly funded insurance are more likely to be diagnosed with advanced prostate cancer [16–19]. Low-income AA men have had higher PSA levels compared to AA men with higher incomes [20]. Furthermore, recent changes in Medicare reimbursement schedules may determine screening applications after age 65 [21], and marital status is one of the most consistent determinants of prostate cancer screening [15]. Thus, screening practices may be determined by race, age, and socioeconomic status (SES), and any investigation of racial disparities in screening practices will require control for SES and age.

The purpose of this cross-sectional study is to describe race-specific prostate cancer screening practices within the past 12 months among a large population of predominately low-income AA and CA men between 40 and 79 years of age. After describing the age and race-specific screening patterns, we evaluate the effect of SES on racial disparities in prostate cancer screening within age groups.

2. Materials and methods

2.1. Study design

The Southern Community Cohort Study (SCCS) is a large-scale prospective cohort study designed to help resolve questions regarding the etiology of lung, breast, colorectal, prostate, and other cancers, as well as to elucidate causes of the disparities in cancer incidence and mortality across racial and urban/rural groups. This cross-sectional analysis of screening and race used baseline data collected from participants at enrollment into the SCCS.

2.2. Recruitment and eligibility

SCCS recruitment strategies include clinic-based recruitment from community health centers (CHC) throughout the southeast. The CHC provide medical and preventive care mainly to medically underserved and lower-income urban and rural areas. Trained interviewers approach potential study subjects at the CHC, inform them about the study, and ask eligible persons to participate after completing a consent process and form approved by the Vanderbilt University and Meharry Medical College Institutional Review Boards. To be eligible, participants must: be between 40 and 79 years of age; be willing to provide their name, address, and telephone number; be English-speaking; and be not under

treatment for cancer within the past year (with the exception of non-melanoma skin cancer).

2.3. Data collection

Eligible participants were interviewed by a trained interviewer using a computer-assisted interview protocol. Baseline data collection included: demographics, income, occupation, use of alcohol and tobacco, diet, disease histories, medications, and a wide range of potential cancer risk factors. The computer-assisted interview included built-in logic checks, skip patterns, and variable-specific range parameters to maximize data quality and completeness.

Initial questions regarding prostate cancer screening included “Have you ever had a PSA blood test?” and “Have you ever had a digital rectal exam?” Interviewers provided clarifying descriptions as needed. Participants had the option of responding “Don’t know,” or refusing to answer either question. Follow-up questions were asked when their last PSA test or DRE occurred. If they had not received a particular screening test within the past 5 years (or had never received a particular test), participants were asked to indicate at least one reason why they had not been screened (i.e., doctor did not recommend, concern for cost, discomfort of test, embarrassment of test, desire to put it off for another time, fear of cancer, other reasons).

2.4. Statistical analysis

After excluding 315 who described themselves as other than AA or CA, 132 who provided unreliable information based on a quality control evaluation by the interviewer and data manager, and 90 who reported a prior diagnosis of prostate cancer, the analytic study population included 12,552 men (10,599 AA and 1,953 CA) enrolled in the SCCS between March 2002 and September 2004. Two indices each for PSA and DRE screening histories were developed. Outcome variables were first created to indicate if men had “Ever” received a PSA test or DRE in their lifetime and, second, to indicate if men had “Recently” received a PSA test or a DRE within the past 12 months from interview. Men responding to screening questions as “Don’t know,” refused to answer screening questions, or who had missing values for these questions were excluded from the analysis (PSA: $n = 776$; DRE: $n = 16$). Age is a critical component of any screening guidelines, and health insurance coverage may change after age 65. Therefore, race-specific screening practices were considered across age categorized as 40–44, 45–49, 50–64, and 65 years or more.

Chi-squared and Mantel-Haenszel tests were used to compare the homogeneity of PSA or DRE screening across categories of race, age, and demographic and SES indices, including annual household income, education, marital status, and health insurance status. Fisher exact test was used for comparisons when any single category had less than 5% of data, and all P values were 2-sided. Multivariable logistic

regression was used to calculate odds ratios (OR) and 95% confidence intervals (95% CI) summarizing the association between screening prevalence and race across SES strata within separate age groups. AA men served as the reference group, so that an OR greater than 1.0 indicates that CA men are more likely screened compared to AA men. A 95% CI that excludes 1.0 can be interpreted as statistically significant at the 5% level. Interactions between race and SES indices were estimated and tested for statistical significance by the use of a cross-product term between race and an SES variable in a model that contained all main-effect terms.

3. Results

Study participants were men age 40–79 years, recruited from CHC throughout the southeastern United States, with the majority being AA (84%) at an average age of 50.5 years (AA: 50.2 years, standard deviation [SD] = 7.9; CA: 52.3 years, SD = 9.1) (Table 1). About 65% of the men had graduated from high school, vocational school, or completed at least some college. Low-income men were over-represented, with more than 65% reporting an annual household income less than \$15,000. About 49% of the study participants did not have any health insurance, and approximately 30% were currently married or living with a partner.

Overall, 56% and 44% of the men reported a prior DRE or PSA test, respectively (Table 2). Totals of 16% and 18% of the men, respectively, reported a DRE or PSA test within the past 12 months. PSA and DRE administrations were significantly and positively associated with CA race, education, income, marriage, and health insurance. Screening practices associated with private and public insurance were similar (all $P > 0.05$). The patterns for “ever” and “recent” PSA test or DRE were generally similar, although the association between a recent DRE and race was not significant.

The Figures illustrate the trends in recent (Fig. 1) or lifetime (Fig. 2) PSA and DRE screening by race across 2-year age groups. Screening prevalences increased with age as expected, however, the racial disparity in screening practices was age-dependent. Fig. 1 suggests that proportionately, between 40 and 49 years of age, more AA men reported a recent PSA or DRE test compared to CA men. Between ages 50 and 64 years, recent PSA testing varied little by race, but AA men were more likely to report a recent DRE. After age 65, CA men were more likely to receive a recent PSA test or DRE. These patterns were less evident for lifetime PSA testing or DRE (Fig. 2).

Table 3 summarizes the age-specific associations between race and prostate cancer screening while controlling for SES. CA men 45–49 years old were significantly less likely to report any prior or recent PSA test ($OR_{adj} = 0.77$ [0.61, 0.97], $OR_{adj} = 0.67$ [0.47, 0.93], respectively). The similarity between the crude and adjusted measures of association suggests that factors besides SES contribute to the screening disparities among these younger men. In addition,

Table 1

Study population summary ($N = 12,550$): The Southern Community Cohort Study

	Number (%)
Age (yrs)	
40–44	3781 (30.1)
45–49	3240 (25.8)
50–64	4702 (37.5)
65–79	827 (6.6)
Race	
AA	10,599 (84.4)
CA	1951 (15.6)
Education	
<9 yrs	1219 (9.7)
9–11 yrs	3214 (25.6)
12 yrs/high school/general equivalency diploma	4519 (36.0)
Technical/vocational	662 (5.3)
Junior college	2053 (16.4)
College 4 yrs	628 (5.0)
Master degree or more	255 (2.0)
Household annual income	
<\$15,000	7967 (65.5)
\$15–\$24,999	2704 (21.6)
\$25–\$49,999	1336 (10.7)
\$50–\$99,999	364 (2.9)
≥\$100,000	54 (0.5)
Refuse/don't Know	125 (1.0)
Marital status	
Married/live with partner	3717 (29.6)
Separated/divorced	4452 (35.5)
Widowed	501 (4.0)
Single, never married	3875 (30.9)
Health insurance*	
No insurance	6186 (49.3)
Private insurance	2232 (17.8)
Public insurance	3975 (31.7)
Other insurance	146 (1.2)

* Mutually exclusive insurance categories created from men reporting any private insurance, only publicly funded insurance including Medicare, Medicaid, and VA/CHAMPUS, or insurance from sources other than private or public sources.

CA men age 50–64 years were significantly less likely to report a recent DRE ($OR_{adj} = 0.78$ [0.63, 0.86]). In contrast, CA men age 65 years or older were significantly more likely to report a recent PSA or DRE in the crude analysis. However, these associations were attenuated and no longer significant after adjustment for demographics and SES.

Table 4 explores the independent associations between SES and recent screening practices. Age was dichotomized at age 50 to support model stability. In separate analyses for each race and age category, variables representing health insurance, marital status, income, and education were included in a single model. Health insurance coverage was significantly associated with recent screening practices within each race and age group, with those without insurance consistently less likely to be screened. Similarly, unmarried men were less likely to receive a recent screening test, with statistically significant associations among men older than age 50. Higher income and education tended to be positively associated with screening, particularly among

Table 2

Percentage of men screened for prostate cancer across demographic and SES indices: The Southern Community Cohort Study

	“Ever” screened*		“Recently” screened ^a	
	PSA Number (%)	DRE Number (%)	PSA Number (%)	DRE Number (%)
All men	5,206 (44.2)	6956 (55.9)	2122 (18.0)	1958 (15.7)
Age (yrs)				
40–44	956 (26.5)	1525 (40.4)	338 (9.4)	371 (9.8)
45–49	1194 (38.9)	1706 (52.9)	461 (15.0)	443 (13.7)
50–64	2432 (55.9)	3045 (65.2)	1032 (23.7)	914 (14.6)
65–79	624 (82.5)	680 (82.8)	291 (38.5)	230 (28.0)
	$P < 0.01^b$	$P < 0.01$	$P < 0.01$	$P < 0.01$
Race				
AA	4372 (43.7)	5823 (55.2)	1773 (17.7)	1651 (15.7)
CA	834 (47.1)	1133 (58.4)	349 (19.7)	307 (15.8)
	$P < 0.01$	$P < 0.01$	$P = 0.05$	$P = 0.85$
Education				
High school ^c or less	3727 (41.5)	5080 (53.1)	1492 (16.6)	1395 (14.6)
More than high school	1479 (53.1)	1876 (64.2)	630 (22.6)	593 (19.3)
	$P < 0.01$	$P < 0.01$	$P < 0.01$	$P < 0.01$
Household annual income				
<\$15,000	3028 (40.8)	4198 (52.9)	1240 (16.7)	1123 (14.2)
\$15–\$24,999	1162 (45.4)	1542 (57.3)	438 (17.1)	412 (15.3)
>\$25,000	961 (57.4)	1141 (65.5)	418 (24.9)	400 (22.9)
	$P < 0.01$	$P < 0.01$	$P < 0.01$	$P < 0.01$
Marital status				
Married/live with partner	1901 (54.8)	2299 (62.3)	790 (22.7)	700 (18.9)
Other	3304 (39.8)	4656 (52.9)	1331 (16.0)	1257 (14.3)
	$P < 0.01$	$P < 0.01$	$P < 0.01$	$P < 0.01$
Insurance ^d				
No insurance	1924 (33.2)	2949 (48.0)	720 (12.4)	694 (11.3)
Private insurance	1171 (54.9)	1385 (62.1)	478 (22.4)	430 (19.3)
Public Insurance	2054 (55.6)	2534 (63.9)	900 (24.4)	808 (20.4)
Other Insurance	53 (38.1)	82 (56.2)	22 (15.8)	24 (16.4)
	$P < 0.01$	$P < 0.01$	$P < 0.01$	$P < 0.01$

* Ever received a PSA test or DRE within lifetime.

^a Received a PSA test or DRE within the past 12 months.^b P value from chi-square test for dichotomous variables, or the Mantel-Haenszel chi-square test to evaluate linear trends across ordered variables.^c Includes vocational or technical training.^d Mutually exclusive insurance categories created from men reporting any private insurance, only publicly funded insurance, including Medicare, Medicaid, and VA/CHAMPUS, or insurance other than from private or public sources.

AA men. A separate modeling approach included interaction terms between race and each SES index within each age group. Only the interaction term between race and marital status for a recent DRE was statistically significant ($P = 0.04$), suggesting that the association between marriage and DRE among CA men older than 50 years was stronger than among AA men.

Participants who did not have a PSA test or DRE within the past 5 years responded to questions about their reasons for not doing so. The lack of a doctor recommendation to have the test was more often reported by CA than AA men, with the racial differences somewhat greater for those under versus older than age 50. For example, among participants younger than 50 years, the lack of a doctor recommendation to have a PSA test was noted by 55% of CA and 46% of AA ($P < 0.01$), and to have a DRE was noted by 52% of CA and 44% of AA ($P < 0.01$). Other reasons for not being screened within the past 5 years, including forgetting to be

screened, fear of screening, desire to put screening off to another time, embarrassment, and concern for discomfort with testing, were rarely reported (less than 8% of unscreened men), and the frequency of responses for each reason was not substantively modified by race or age.

3.1. Comment

We investigated prostate cancer screening practices between predominantly low-income AA and CA men residing in the southeastern United States. Racial differences in screening practices were age-dependent. AA men younger than age 50 were more likely to report a recent PSA test, and AA men younger than age 65 were more likely to report a recent DRE. Enhanced PSA testing among AA men was independent of SES and consistent with recommendations to physicians that AA men be offered prostate cancer screening examinations starting at

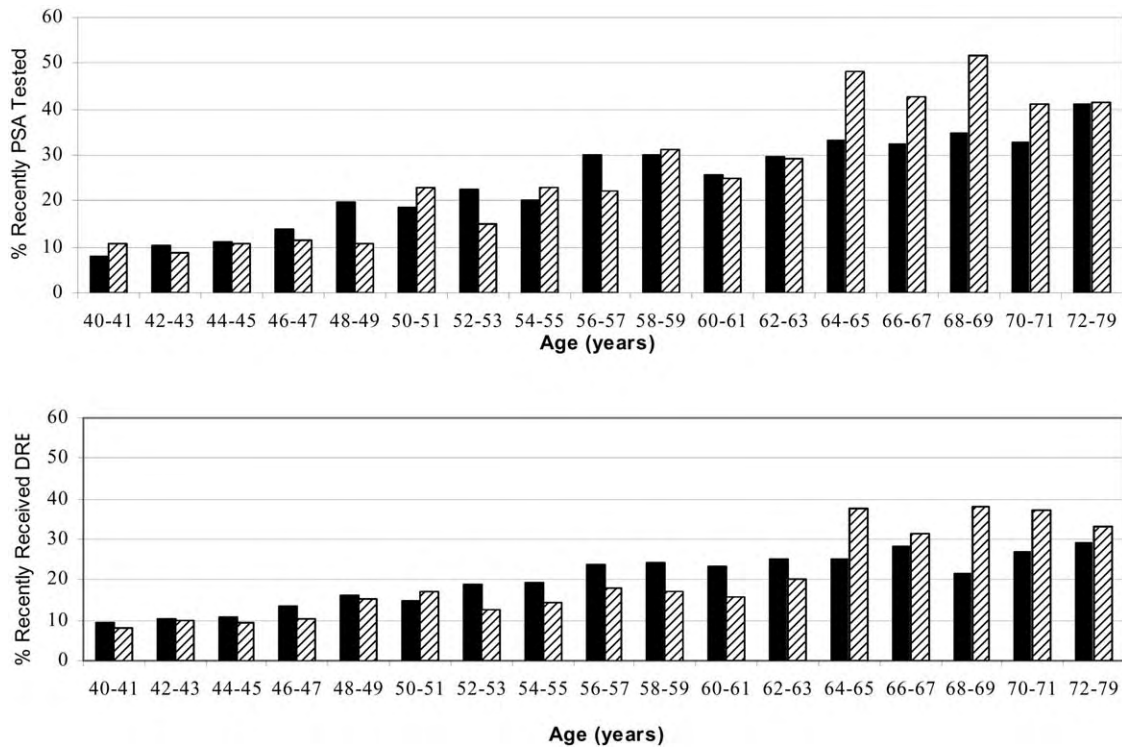


Fig. 1. Percentage of African-Americans (solid) and Caucasians (striped) receiving a prostate specific antigen (PSA) test or digital rectal examination (DRE) within the last 12 months by age: The Southern Community Cohort Study.

age 45 years. After age 65, CA men were significantly more likely to receive a recent PSA test or DRE, however, adjustment for SES and demographic factors reduced this disparity.

A strength of this study is the assembly of a large group of more than 12,000 participants, from generally similar socioeconomic circumstances, in the age range in which prostate cancer screening is relevant. Information was col-

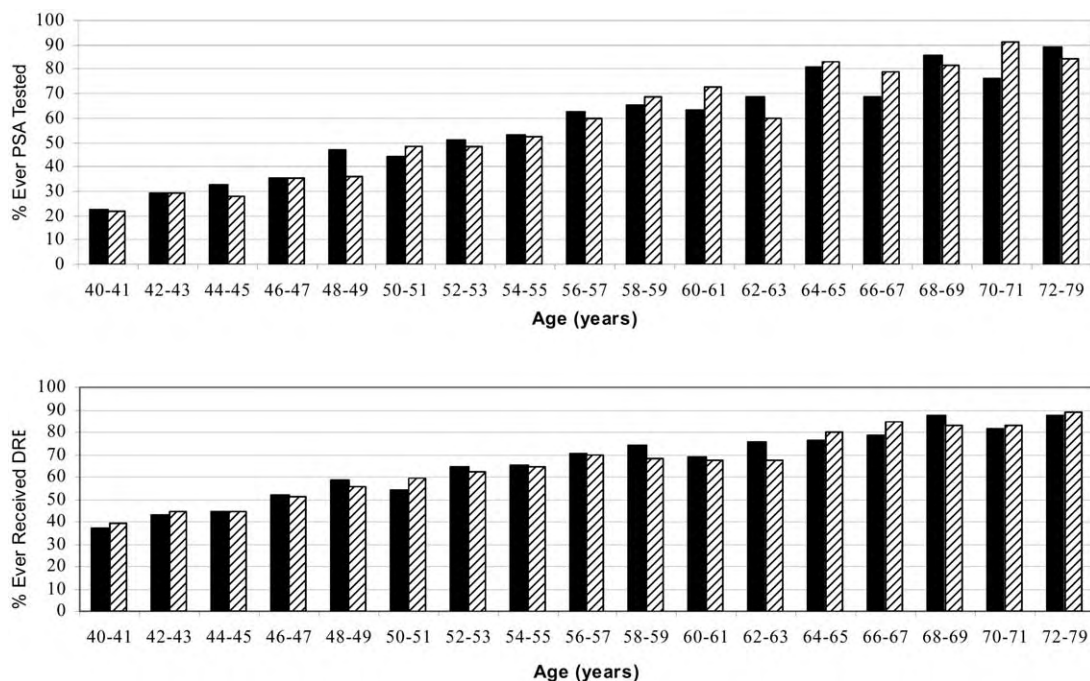


Fig. 2. Percentage of African-Americans (solid) and Caucasians (striped) ever receiving a prostate specific antigen (PSA) test or digital rectal examination (DRE) by age: The Southern Community Cohort Study.

Table 3

Association between race and prostate cancer screening by age group: The Southern Community Cohort Study

	Age (yrs)	AA Number (%)	CA Number (%)	OR (95% CI)*	OR (95% CI) ^a
PSA Ever ^b	40–44	835 (26.8)	121 (25.2)	0.92 (0.74, 1.15)	0.96 (0.76, 1.19)
	45–49	1062 (39.5)	132 (34.7)	0.81 (0.65, 1.01)	0.77 (0.61, 0.97)
	50–64	2018 (55.4)	414 (58.1)	1.11 (0.94, 1.31)	1.00 (0.84, 1.18)
	65–79	457 (81.8)	167 (84.8)	1.24 (0.80, 1.94)	1.01 (0.64, 1.61)
Recent ^c	40–44	292 (9.4)	46 (9.6)	1.03 (0.74, 1.42)	1.09 (0.78, 1.52)
	45–49	418 (15.6)	43 (11.3)	0.69 (0.49, 0.97)	0.67 (0.47, 0.93)
	50–64	860 (23.6)	172 (24.1)	1.02 (0.85, 1.24)	0.95 (0.78, 1.10)
	65–79	203 (36.3)	88 (44.7)	1.42 (1.01, 1.97)	1.23 (0.87, 1.74)
DRE Ever	40–44	1308 (40.2)	217 (41.2)	1.07 (0.88, 1.29)	1.09 (0.90, 1.32)
	45–49	1485 (52.9)	221 (52.3)	0.97 (0.79, 1.19)	0.94 (0.76, 1.15)
	50–64	2530 (65.1)	515 (65.5)	1.02 (0.87, 1.20)	0.95 (0.81, 1.24)
	65–79	500 (82.2)	180 (84.5)	1.18 (0.77, 1.80)	1.00 (0.64, 1.56)
Recent	40–44	325 (10.0)	46 (8.9)	0.88 (0.63, 1.21)	0.90 (0.65, 1.26)
	45–49	390 (13.9)	53 (12.5)	0.89 (0.65, 1.21)	0.90 (0.65, 1.23)
	50–64	779 (20.1)	135 (17.2)	0.83 (0.67, 1.01)	0.78 (0.63, 0.86)
	65–79	157 (25.8)	73 (34.3)	1.49 (1.07, 2.10)	1.33 (0.93, 1.89)

* OR summarizing likelihood that CA men are screened compared to AA men. OR 1.0 indicates CA men more likely screened, while OR < 1.0 indicates AA men more likely screened. A 95% CI that excludes 1.0 can be interpreted as a statistically significant association at the 5% level.

^a Adjusted for insurance source, marriage/partner, annual household income, and education.

^b Ever received a PSA test or DRE within lifetime.

^c Received a PSA test or DRE within the past 12 months.

lected in a standardized fashion using a highly structured questionnaire, and covers a period when guidelines for PSA and DRE screening have been established. One limitation of this study concerns the use of self-reported screening histories. Jordon et al. [22] administered a prostate cancer questionnaire to 271 patients with an appointment at a family practice and compared responses to their medical

charts. Concordance for reporting a DRE and PSA within the past 2 years was 68% and 71%, respectively. A similar medical chart review study found a 74% agreement [23]. The moderate level of consistency was attributed to incorrect timeframe assessment, lack of knowledge about prostate cancer screening, and poor medical chart documentation. Unfortunately, DRE often remain undocumented, and

Table 4

Association between demographic/SES factors and prostate cancer screening within the past 12 months (OR and 95% CI*): The Southern Community Cohort Study

		<50 Years		≥50 Years	
		AA	CA	AA	CA
PSA	No insurance	0.56 (0.48, 0.66)	0.44 (0.28, 0.69)	0.59 (0.51, 0.69)	0.56 (0.41, 0.78)
	Not married or living with partner	0.88 (0.73, 1.06)	0.91 (0.56, 1.46)	0.80 (0.69, 0.93)	0.70 (0.51, 0.95)
	Income >\$25,000/yr	1.30 (1.04, 1.64)	1.11 (0.59, 2.08)	1.40 (1.13, 1.74)	1.03 (0.68, 1.54)
	Any college education	1.48 (1.23, 1.77)	1.50 (0.91, 2.46)	1.32 (1.11, 1.57)	1.12 (0.80, 1.56)
DRE	No insurance	0.59 (0.50, 0.69)	0.49 (0.32, 0.75)	0.64 (0.55, 0.75)	0.65 (0.46, 0.99)
	Not married or living with partner	1.05 (0.87, 1.28)	0.81 (0.52, 1.26)	0.89 (0.76, 1.05) ^a	0.57 (0.42, 0.79)
	Income >\$25,000/yr	1.78 (1.42, 2.22)	1.49 (0.84, 2.65)	1.47 (1.18, 1.83)	1.02 (0.66, 1.58)
	Any college education	1.30 (1.08, 1.56)	1.18 (0.73, 1.90)	1.24 (1.03, 1.48)	1.13 (0.79, 1.60)

* OR and 95% CI adjusted for race and the 4 factors listed in the table (insurance, marital status, income, education). OR 1.0 indicates that the factor is associated with an increased likelihood of being screened, while OR < 1.0 indicates that the factor is associated with decreased likelihood of being screened. A 95% CI that excludes 1.0 can be interpreted as a statistically significant association at the 5% level.

^a $P_{\text{interaction}} = 0.04$ for interaction between race and marriage on recently receiving a DRE.

PSA tests performed at other clinics would not be captured in a single chart review. Our standardized interview-based approach and multivariable adjusted modeling approach should reduce the impact of reporting errors associated with health illiteracy, comprehension, or patient education.

The SCCS recruits from CHC tend to be of considerably lower income than the general population. Nevertheless, prostate cancer screening practices were comparable to other large-scale surveys with age-specific data. The 2000 National Health Interview Survey (NHIS) included 513 AA men and found a higher recent PSA prevalence among AA men between 45 and 49 years (AA: 16.8%; CA: 10.4%; $P = 0.055$) [24], similar to our study with more than 10,000 AA men (AA: 15.6%; CA: 11.3%). The 1998 NHIS found that 43% and 52% of AA and CA men, respectively, older than age 50 reported a DRE within the past 2 years [12]. Recalibration of our data to the 2-year NHIS definition found that 52% of CA older than age 50 reported a recent DRE, identical to the NHIS rate in 1998, while DRE use among AA men in the SCCS was somewhat higher (59%) than NHIS estimates. In 1998, 31% and 38% of AA and CA men, respectively, receiving Medicare benefits received a PSA test [14]. Of men older than age 65 in our study, 36% and 45% of AA and CA men, respectively, reported a PSA test within the past 12 months. These values may be more comparable than apparent because PSA use among Medicare-eligible AA men was increasing in 1998 [14], and Medicare started to reimburse for PSA screening tests in 2000 [21]. Despite the differences in insurance coverage, geographic region, income, and study periods, DRE and PSA rates among AA and CA men in our study appeared, for the most part, comparable to rates observed in national surveys or insurance registries, lending further support to the self-reported screening data.

Consistent with prior research, we found that CA men older than age 65 were significantly more likely to report a recent PSA test or DRE [14]. However, adjustment for demographic and SES factors, including education, insurance, marital status, and income, reduced this disparity. Similar cofactors were significantly associated with AA and CA participation in a free cancer screening program [15], among insured military veterans [25], and in an analysis of Medicare files after adjustment for the type of insurance [26]. Interestingly, the 1997 Behavioral Risk Factor Surveillance System telephone survey (New York State) reported no racial disparity in PSA testing [27], although 94% of men surveyed had health insurance. We saw no decline in screening practices among older participants, consistent with previously noted age-independent screening decisions among older men [28]. These results suggest that economic or social factors, and not a race-specific factor, contribute to differences in screening practices after age 65 years.

Each SES component independently associated with PSA testing may represent a unique set of attributes. For example, marital status may reflect a complex relationship between behavioral, social, and economic factors that may

underlie the association between marriage and screening practices. Our data raise the possibility that these constructs might affect DRE practices differently between AA and CA men, but this single significant interaction may be a chance finding due to the multiple comparisons we made. It is interesting that income and insurance coverage were associated with prostate cancer screening in this study. CHC maintain services through government grants, insurance reimbursement, and a sliding-scale payment schedule, and it is unclear how patients might perceive income and insurance as barriers in this context. Assessment of relationships between prostate cancer screening and social support structures, self-efficacy to make health care decisions, and individual perceptions of health and disease might help address these issues.

The PSA test and DRE are imperfect screening approaches that have not been conclusively shown to reduce mortality. Although these procedures detect tumors at an earlier stage, the PSA test is not specific for cancer, and the DRE lacks the sensitivity to detect localized and nonpalpable tumors. As treatments of nonlethal disease impose serious comorbidities [29,30], administration of prostate cancer screening procedures is highly controversial. The U.S. Preventive Services Task Force and the American College of Physicians have withheld screening recommendations until the relationship between screening and mortality is better understood. However, the ACS, the American Urological Association (AUA), and the American College of Radiology (ACR) have recommended that counseling and annual PSA/DRE screening be offered to men starting at 50 years. Furthermore, the ACS, AUA, and ACR recommend men at high risk for prostate cancer, including AA men or men with a family history, should be offered counseling and screening starting at age 45 years [31].

We found that AA men between 45 and 49 years of age were significantly more likely to report a recent PSA test compared to age-comparable CA men. This screening difference remained statistically significant after controlling for SES indices. Furthermore, younger CA men were significantly more likely to report that their physician had not recommended a PSA test compared to younger AA men, while physician recommendations were more comparable across race among men older than age 50. Few men reported cost, embarrassment, or discomfort as the principal barriers to screening. Although overall screening rates were low among these younger men, racial differences in screening before age 50 years appear consistent with ACS/AUA/ACR guidelines on prostate cancer screening.

Our results are largely descriptive, however, the modest preference for AA screening among younger men suggests that delayed diagnosis may not be strongly associated with prostate cancer racial disparities among CHC patients younger than age 65. Perhaps genetic, lifestyle, or treatment factors contribute more to prostate cancer racial disparities in younger men with access to screening. Furthermore, delayed detection may retain a role among older CHC

patients. Future prospective analyses will investigate the relative contributions of genetic, lifestyle, economic, and health service risk factors on race and age-specific prostate cancer among these low-income men.

4. Conclusions

There have been few opportunities to investigate race and prostate cancer screening, particularly among low-income men. This large-scale evaluation of prostate cancer screening found age-specific screening practices in this population consistent with reports from several large investigations. CA men older than age 65 were significantly more likely to receive a recent PSA test, however, this disparity was considerably reduced following SES adjustment. Although screening rates among men younger than 50 years were low, AA men were significantly more likely to receive a recent PSA test, suggesting that guidelines for the increased screening of AA beginning at age 45 are being implemented at the community level.

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